STUDY OF THYROID AND LIPID PROFILE IN CHRONIC KIDNEY DISEASE

Dissertation submitted to

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In partial fulfillment for the Degree of

(BRANCH- I) M.D. (GENERAL MEDICINE)

TIRUNELVELI MEDICAL COLLEGE AND HOSPITAL

TIRUNELVELI – 627011

MAY 2019

BONAFIDE CERTIFICATE

This is to certify that the Dissertation entitled **"STUDY OF THYROID AND LIPID PROFILE IN CHRONIC KIDNEY DISEASE"** submitted by **Dr. AKBARSHA.A.** to The Tamilnadu **Dr. M.G.R. Medical University, Chennai,** in partial fulfillment for the award of **M.D. Degree Branch-I(General Medicine)** is a bonafide research work carried out by him under my guidance and supervision during the course of study 2016-2019. This dissertation partially or fully has not been submitted for any other degree or diploma of this university or other.

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This is to certify that the Dissertation Entitled **"STUDY OF THYROID AND LIPID PROFILE IN CHRONIC KIDNEY DISEASE"** presented herein by **Dr. AKBARSHA.A.** is an original work done in the Department of General Medicine, Tirunelveli Medical College and Hospital, Tirunelveli for the award of Degree of M.D. (Branch I) General Medicine. During his Post graduate degree course period from 2016 -2019. This work has not formed the basis for previous award of any degree.

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DECLARATION

I solemnly declare that the dissertation titled **"STUDY OF THYROID AND LIPID PROFILE IN CHRONIC KIDNEY DISEASE"** is prepared by me. The dissertation is submitted to The Tamilnadu Dr.M.G.R. Medical University towards the partial fulfillment of requirements for the award of M.D. Degree (Branch I) in General Medicine. I also solemnly declare that this bonafide work or a part of this work was not submitted by me or any others for any award, degree, diploma to any university, found either in India or abroad.

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PROTOCOL TITLE: STUDY OF THYROID AND LIPID PROFILE IN CHRONIC KIDNEY DISEASE
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DESIGNATION OF PRINCIPAL INVESTIGATOR: PG STUDENT
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Dear, Dr.A.AKBARSHA,, MBBS.., The Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during the IEC meeting held on 10.03.2017

THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

1.	TIREC Application Form	☐
2.	Study Protocol	☐
3.	Department Research Committee Approval	☐
4.	Patient Information Document and Consent Form in English and Vernacular Language	☐
5.	Investigator's Brochure	☐
6.	Proposed Methods for Patient Accrual Proposed	☐
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8.	Insurance /Compensation Policy	☐
9.	Investigator's Agreement with Sponsor	☐
10.	Investigator's Undertaking	☐
11.	DCGI/DGFT approval	☐
12.	Clinical Trial Agreement (CTA)	☐
13.	Memorandum of Understanding (MOU)/Material Transfer Agreement (MTA)	☐
14.	Clinical Trials Registry-India (CTRI) Registration	☐

THE PROTOCOL IS APPROVED IN ITS PRESENTED FORM ON THE FOLLOWING CONDITIONS

1. The approval is valid for a period of 2 year/s or duration of project whichever is later
2. The date of commencement of study should be informed
3. A written request should be submitted 3weeks before for renewal / extension of the validity
4. An annual status report should be submitted.
5. The TIREC will monitor the study
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   a) The exact alteration/amendment should be specified and indicated where the amendment occurred in the original project. (Page no. Clause no. etc.)
   b) The PI must comment how proposed amendment will affect the ongoing trial. Alteration in the budgetary status, staff requirement should be clearly indicated and the revised budget form should be submitted.
   c) If the amendments require a change in the consent form, the copy of revised Consent Form should be submitted to Ethics Committee for approval. If the amendment demands a re-look at the toxicity or side effects to patients, the same should be documented.
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Last but not the least; I thank **Almighty God**, for giving me wisdom, favours and blessings.

CERTIFICATE- II

This is to certify that this dissertation work title **" STUDY OF THYROID AND LIPID PROFILE IN CHRONIC KIDNEY DISEASE IN TIRUNELVELI MEDICAL COLLEGE HOSPITAL"** of the candidate **Dr.AKBARSHA.A**, with registration Number **201611351** for the award of **M.D.,** Degree in the branch of **GENERAL MEDICINE (I).** I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion page and result shows **3% percentage** of plagiarism in the dissertation.

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LIST OF TABLES AND CHARTS

ABBREVIATION

ACEI	-	Angiotensin Converting Enzyme Inhibitors
Apo	-	Apolipoprotein
ARB’s	-	Angiotensin Receptor Blockers
BP	-	Blood Pressure
CGN	-	Chronic Glomerulonephritis
CIN	-	Chronic Interstitial Nephritis
CKD	-	Chronic Kidney Disease
CVD	-	Cardio Vascular Disease
DIT	-	Diiodotyrosine
DM	-	Diabetes Mellitus
ECG	-	Electro Cardiogram
ESRD	-	End Stage Renal Disease
GFR	-	Glomerular Filteration Rate
HD	-	Hemodialysis
HDL-C	-	High Density Lipoprotein Cholesterol
HTN	-	Hypertension
ID No	-	Patient Identification Number
K/DOQI	-	Kidney Disease Outcome Quality Initiative
K+	-	Potassium
LCAT	-	Lecithin Cholesterol Acyl Transferase
LDL-C	-	Low Density Lipoprotein Cholesterol

LK	-	Left Kidney
LPL	-	Lipoprotein Lipase
LVH	-	Left Ventricular Hypertrophy
MDRD study	-	Modification of Diet in Renal Disease study
MIT	-	Monoiodotyrosine
Na+	-	Sodium
PD	-	Peritoneal Dialysis
PMP	-	Per Million Population
PTH	-	Parathyroid Hormone
RK	-	Right Kidney
rT3	-	Reverse T3
Sd LDL	-	Small Dense Low Density Lipoprotein
T3	-	Triiodothyronine
T4	-	Thyroxine
TBG	-	Thyroxine Binding Globulin
TC	-	Total Cholesterol
TGL/TG	-	Triglycerides
TRH	-	Thyrotropin Releasing Hormone
TSH	-	Thyroid Stimulating Hormone
USG	-	Ultra Sonogram

INTRODUCTION

1. INTRODUCTION

Chronic kidney disease (CKD) encompasses group of distinct pathophysiological processes which are associated with abnormal kidney functioning and progressively reducing Glomerular Filtration rate (GFR).

Various pathological processes in CKD ultimately results in loss of Renal metabolic, excretory, endocrine, and synthetic functions due to accumulation of various protein nitrogenous substances.

The widespread cause of mortality in patients with CKD is spectrum of cardiovascular diseases. The prevalence of cardiovascular morbidity in patients of age group 25-34 years with CKD is 500 times that of people without CKD in similar age group and race.

The initial stages of CKD are mostly managed by Primary Care Physicians and they have a pivotal role in delaying the progression of CKD to ESRD by addressing various co-morbidities associated with CKD by identifying and intervening them early.

Two of such important co-morbidities being lipid dysfunction and Thyroid dysfunction in patients with CKD.

Hyperlipidemia , an abnormally high level of lipids in blood ,is a well known risk factor for early Atherosclerosis causing various cardiovascular diseases ,is frequently seen in patients with CKD.

Indian studies demonstrating pathophysiological relationship of CKD with Lipid profile have quoted almost nil Lipid profile abnormalities in

CKD to pathophysiologically significant alterations in lipid profile in patients with CKD like high triglycerides and low HDL level.

B Shah, S Nair studied the occurrence of lipid profile abnormalities in CKD and have demonstrated the significant hypertriglyceridemia in patients with CKD.

Increased level of triglycerides, total cholesterol and low levels of HDL-C in patients with CKD managed conservatively has been shown in study by Sumathi M.E, Manjunath, M.Tempad.

There is also an evidence of thyroid hormone dysfunction in patients with CKD.CKD causes alteration in synthesis, secretion, metabolism & elimination of Thyroid hormones.

Iodine an important element in the synthesis of thyroid hormone is removed from circulation by glomerular filtration under physiological conditions .In CKD, the progressively decreasing GFR leads to accumulation of Iodine in blood which ultimately leads to decreased thyroid hormone synthesis by 'Wolff Chaikoff effect'.

This results in subnormal levels of serum total & free T_3 concentration and normal reverse T_3 & free T_4 levels. But, TSH level is mostly unaltered in CKD. Patients may also have symptoms of hypothyroidism in CKD.

Studies in the past have demonstrated all types of thyroid abnormalities like hypothyroidism, hyperthyroidism and euthyroidism in

patients with CKD. The prevalence of hypothyroidism is 0.9% in patients with ESRD. Goitre is also noted in patients with CKD.

Because of this pathologically significant occurrence of dyslipidemia and thyroid abnormalities in patients with CKD, a prospective study of lipid profile & thyroid abnormalities in CKD has been undertaken in the Department of General Medicine, Tirunelveli Medical College and hospital, Tirunelveli.

AIMS AND OBJECTIVES

2. AIMS AND OBJECTIVES OF THE STUDY

- To determine Thyroid profile of CKD patients and compare them with healthy controls

- To determine Serum Lipid profile of CKD patients and compare them with healthy controls

REVIEW OF LITERATURE

3. REVIEW OF LITERATURE

3.1 FUNCTIONS OF THE KIDNEY

The important functions of the kidney are:

- Excretion of waste products of metabolism, toxins and few drugs.
- Strict regulation of fluid and electrolyte balance.
- Maintenance of acid – base balance.
- Maintenance of body fluid osmolality and electrolyte composition.
- Maintaining blood pressure.

It also contributes to secretion, metabolism and excretion of few hormones. Its important endocrine functions are production of renin, erythropoietin, prostaglandins and endothelins.

The important metabolic function of the kidney is the 1hydroxylation of 25 hydroxy D3 and aids in vitamin D synthesis. It regulates of erythrocyte production by secreting erythropoietin.

DETERMINANTS OF GFR[1]

Cockcroft and Gault formula is most commonly used to estimate GFR.

It goes as:

Estimated creatinine clearance in ml/min = (140 – age) X Lean body weight (kg) 72X plasma creatinine (mg/dl).

Multiply by 0.85 for women.

3.2 CHRONIC KIDNEY DISEASE

Definition

Signs of kidney damage for more than or equal to three months as explained by anatomical or physiological abnormalities of the kidney, with or without reduction in GFR.

GFR value below 60 ml/min/1.33m^2 for more than or equal to three months with or without other signs of kidney damage**.**

Causes of chronic kidney disease

The most prevalent cause of chronic kidney disease in developed countries is diabetic glomerulosclerosis while in developing countries being primary glomerulonephritis.

Major etiologies of CKD

- DiabeticNephropthy
- Glomerulonephritis
- Hypertension – associated CKD
- Autosomal dominant polycystic kidney disease
- Medullary cystic kidney
- Tubulointerstitial nephropathy. Etc.,

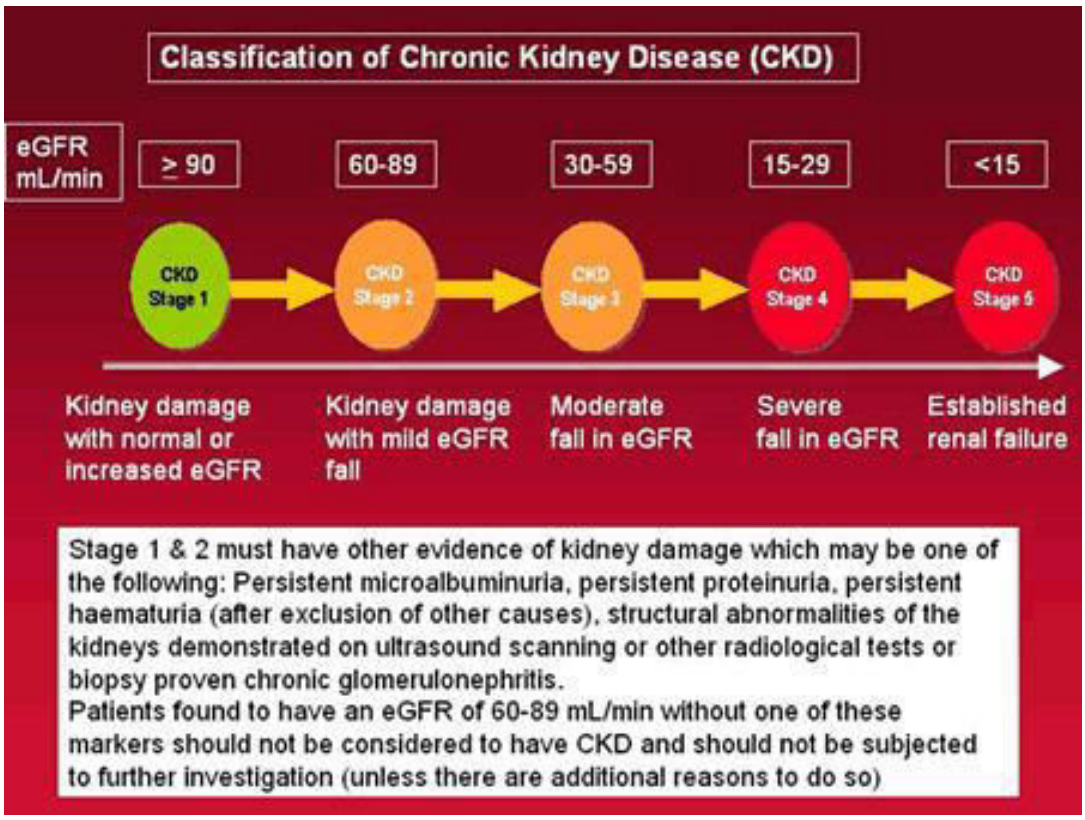
STAGES OF CKD:[2]

Stage	Description	GFR (mL/min/1.73 m^2)
1	Kidney damage	≥90
	With normal or ↑ GFR	
2	Kidney damage	60–89
	With mild ↓ GFR	
3	Moderate ↓ GFR	30–59
4	Severe ↓ GFR	15–29
	Kidney failure	<15 (or dialysis)

Chronic kidney disease is defined as either kidney damage or GFR <60 mL/min/1.73 m^2 for ≥3 months. Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

KDIGO: The Kidney Disease Improving Global Outcomes, CKD: Chronic kidney disease, GFR: Glomerular filtration rate

CLASSIFICATION OF CKD:



CLASSIFICATION OF CKD BY PATHOLOGY AND ETILOGY:

PATHOLOGY:	ETIOLOGY:
➢ Diabetic Glomerulosclerosis ➢ Glomerular diseases(Primary and secondary) Pproliferative Glomerulonephritis ➢ Minimal change disease ➢ Membranous Nephropathy ➢ Focal Glomerular sclerosis ➢ Fibrillary Glomerular disease ➢ Hereditary Nephritis ➢ Diseases affecting vessels: large size vessels Medium size vessel (Nephrosclerosis) Small size vessels (Microangiopathy) ➢ Tubulointerstitial diseases: Reflux nephropathy Tubulointerstitial nephritis Obstructive nephropathy Myeloma kidney ➢ Cystic Kidney diseases: ➢ Polcystic kidney disease ➢ Von-Hippel Lindau disease ➢ Tuberous sclerosis ➢ Medullary cystic Kidney	➢ Diabetes mellitus ➢ commonly idiopathic ➢ Hypertension ➢ SLE,Bacterial Endocarditis,HIV, ➢ Hepatitis B and C virus, ➢ Hodgkin,s disease ➢ Drug toxicity ➢ Solid tumours, ➢ Light chain diseases ➢ Amyloidosis ➢ Alport's syndrome ➢ Aortoarteritis ➢ Renal artery stenosis ➢ Vasculitis ➢ Hemolytic Uraemic syndrome ➢ Sickle cell disease with or without crisis ➢ Vesico Ureteric Reflux disease ➢ Stones,Malignancy,Prostatic enlargement ➢ Sarcoidosis ➢ Infections, drugs and toxins ➢ Multiple Myeloma

				Persistent albuminuria Categories, Descriptions, and Ranges		
Albuminuria Category				A1	A2	A3
Albuminuria Description				Normal to mildly increased	Moderately increased	Severely increased
Albumin-to-creatinine ratio Ranges mg creatinine/g albumin				<30	30-300	>300
GFR Categories, Descriptions, and Ranges	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			
	GFR Category	GFR Description	GFR Ranges mL/min/1.73m^2			

Progression of CKD

Color	Interpretation
	Low risk, if no other markers of kidney disease, no CKD
	Moderately increased risk
	High risk
	Very high risk

Modified with permission from Kidney International. Levey AS, de Jong PE, Coresh J, et al. The definition, classification, and prognosis of chronic kidney disease, a KDIGO controversies report. *Kidney Int.* 2011; 80: 17-28.

PATHOPHYSIOLOGY OF CKD:

The two underlying pathophysiologic manifestations in CKDS are:

1. Mechanisms that initiate pathological processes in CKD specific to particular etiology
2. Mechanisms involving hypertrophy & hyperfiltration of the left out viable nephrons following long term reduction in renal mass, whatever may be the cause .
3. Various mediators attributed to nephron loss are:
    - Cytokine
    - Various Vasoactive hormones

Growth factors

Finally short term adaptations like hypertrophy and hyperfiltration in the remaining viable nephrons becomes maladaptive as the pressure increases and flow within the nephron susceptible to glomerular architectural distortion, podocyte dysfunction and interruption of filtration barrier which ultimately leads to sclerosis and dropout of remaining viable nephrons. Increase in renin- angiotensin system contributes to both initiative and subsequent maladaptive hypertrophy and sclerosis.

The peculiar property of kidney in CKD is the compensatory and adaptive mechanism which makes the condition asymptomatic until the GFR falls to 10-15 ml/min and life sustaining renal excretory and homeostatic functions continues until GFR is less than 5 ml/minute making

the disease truly a silent killer. Different Hypotheses explaining the pathological processes in CKD are:

INTACT NEPHRON HYPOTHESIS:

In CKD, there is progressive loss of functioning nephrons. The remaining few viable nephrons try to compensate for the lost nephrons and tends to hypertrophy which results in summed up work load, so overall functional loss is reduced. This adaptive mechanism is called as compensatory hyperfiltration.

A study conducted in renal transplant donors, there is increased glomerular filtration rate upto 40% and increase in renal plasma flow in the remaining kidney within weeks after nephrectomy. The GFR increases to about 70% of prenephrectomy range.

Increased perfusion of remaining viable nephrons causes production of increased volume of glomerular filtrate. The tubules responds to increased changes by excreting fluids and solutes in larger amounts which helps in maintaining external balance. This efficient integration of functions of glomerulus and tubules is known as “Glomerulotubular balance” which is preserved until later stages of the disease.

TRADE OFF HYPOTHESIS:

Trade off hypothesis states that, adaptation emerging in CKD may control one abnormality, but only in such a way to produce other changes which is characteristic of uraemic syndrome. The mechanism of which is not precisely known. It is described in hormones like atrial natureteric peptide,vasopressin, parathromone and solutes including sodium, potassium, phosphate and others.

MIDDLE MOLECULE HYPOTHESIS:

Patients who are all treated with maintenance peritoneal dialysis, have a conflict between the degree of azotemia and presentation of the disease symptoms. In patients undergoing maintanence peritoneal dialysis, inspite of higher renal parameters the symptoms of uraemia are mild and they are less prone to the development of peripheral neuropathy when compared with the same counterparts undergoing hemodialysis.

This suggests that toxicity is mainly dependant upon the presence of high molecular weight substances which are readily removed in Peritoneal dialysis (50-500 daltons) than in hemodialysis.

FLUID, ELECTROLYTES AND ACID BASE DISORDERS

Sodium and water homeostasis

In CKD patients, ECF (extracellular fluid) volume is maintained in the physiological range till the very late stages of CKD. Fractional excretion of sodium is increased in patients with CKD so that absolute sodium excretion is unchanged until late stages.

Total body content of sodium is important determinant in the extracellular fluid volume, so any impairment in sodium balance will lead to volume overload or volume depletion .Volume depletion is caused by sudden salt restriction in CKD which is frequently seen with tubulointerstitial diseases (salt losing nephropathies). On contrary, retention of sodium leads to peripheral edema, cardiac failure and arterial hypertension.

Diuretics are frequently used to cause natriuresis in CKD patients. Thiazide diuretics have a minimal role. Loop diuretics in higher doses are recommended in CKD. Metalazone can also be combined with loop diuretics, which inhibits sodium chloride co–transporter present in the distal convoluted tubule of the kidney, favouring increased sodium excretion.

Potassium homeostasis:

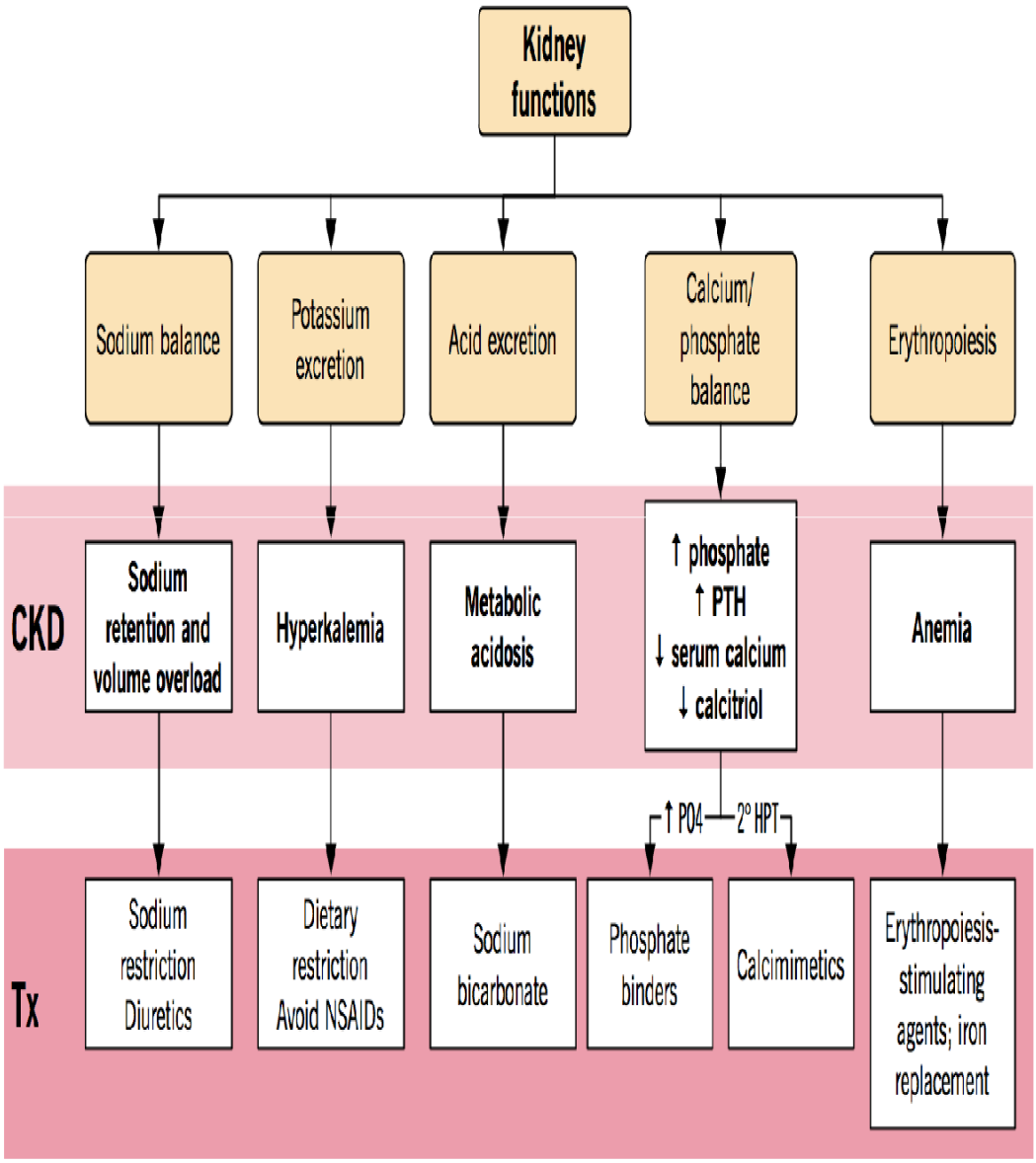
In CKD, excretion of potassium in kidneys is reduced which is in proportion to loss of glomerular filtration. The adaptive mechanisms being increased secretion of aldosterone and significantly high extrarenal

(intestinal) excretion of potassium to maintain potassium homeostasis until the glomerular filtration falls to10 ml/minute.

Drugs such as ACEI, ARBs, aldosterone antagonist, NSAIDs frequently cause hyperkalemia in CKD. The other causes include diet rich with potassium, hemolysis, Hemorrhage, high protein breakdown, metabolic acidosis. hyperkalemia is managed with dextrose with insulin, salbutamol (beta 2 agonist) nebulisation, 10% calcium gluconate (if electrocardiographic changes are obvious).

Hypokalemia is rare in CKD, if it present, it is mainly seen with excessive diuretic therapy, extrarenal (gastrointestinal) loss, reduced intake of potassium.

Complications of CKD



Metabolic acidosis

Non anion gap metabolic acidosis is frequently seen in earlier stages of CKD. In Later stages of CKD, the total daily urinary acid excretion is reduced to 30 – 40 mmol and anion gap of not more than 20mEq/L is seen frequently.

Changes in Haematological System:[3]

In CKD, there is normocytic normochromic anaemia due to decreased renal synthesis of erythropoietin, a hormone which involved in stimulation of bone marrow red blood cell production.

The various causes of anaemia in CKD are:

- Decreased RBC life span
- Iron deficiency
- Vitamin B12 and folate deficiency
- Uraemia induced platelet dysfunction and bleeding
- Chronic inflammation
- Aluminium toxicity
- Renal osteodystrophy and bone marrow fibrosis
- Hyperparathyroidism
- Hemorrhage

Bone Changes[4]

Mineral metabolism is affected in CKD leading to metabolic bone disease causing dual skeletal and extraskeletal abnormalities

Mineral and bone metabolism disturbances in CKD manifests as: Calcium, phosphorous, parathormone and vitamin D metabolic dysfunction. Abnormalities in bone turn over, mineralisation. Vascular and soft tissue calcification.

CKD and heart:

In CKD, the most common cause of morbidity and mortality is cardiovascular diseases. Myocardial ischemia, Uremia, left ventricular hypertrophy, which occur in CKD can cause congestive cardiac failure and pulmonary edema, due to raised permeability of pulmonary alveolar capillary membrane in lungs.

Peripheral neuropathy:

The classical presentation peripheral neuropathy is seen in advanced stages (stage IV and V) of CKD. Sensory neuropathy is more common than motor neuropathy. The lower extremities are more commonly affected than upper extremities and distal part of limb is more affected than proximal part.

Uraemic encephalopathy:

It manifests as acute or subacute organic brain syndrome when glomerular filtration falls to less than 10% of normal. The clinical symptoms & signs of uraemic encephalopathy includes altered level consciousness, psychomotor disturbances and disturbances of thinking, memory, speech, emotion and perception.

Restless leg syndrome:

The restless leg syndrome is one of the manageable causes of sleep disturbance in end stage renal disease. It is a neurological motor movement disorder of limbs associated with sleep disruption. It presents as unpleasant sensation in legs and feet requiring frequent limb movement.The urge to move limbs is more during rest and is relieved with movements.

Gastrointestinal abnormalities:

Uraemic gastritis, peptic ulcer disease and mucosal ulcerations can occur in the gastrointestinal tract in patients with CKD.

Metabolic disturbances:

Fasting increased insulin production can cause spontaneous hypoglycemia in patients with end stage renal disease . Insulin requirement may be reduced in late stages of CKD. The other abnormalities being impaired glucose tolerance and decreased insulin sensitivity.

Dermatological abnormalities:

The frequent dermatological changes seen in CKD include pruritis and skin excoriation. Dysfunctional calcium and phosphorus metabolism can cause vascular and soft tissue calcification which ends uo in skin and soft tissue necrosis. It is known as calciphylaxis seen solely due to secondary hyperparathyroidism.

3.3 THYROID

ANATOMY OF THYROID GLAND:

The thyroid gland is made of two lobes united by an isthmus. It lies in front of trachea in between suprasternal notch and cricoid cartilage. Weight being 12 to 20 grams and is larger in females than in males. Two pairs of parathyroid glands are situated back at each pole of thyroid gland, which synthesizes and secretes parathormone.

PHYSIOLOGY OF THYROID HORMONES:

The hormones produced and secreted by thyroid gland are T3 (Triiodothyronine) and T4 (Thyroxine). Thyroid hormones play a important role in cell differentiation during development and maintainence of metabolic homeostasis in adults[5]

. The secretion of T3 and T4 are mainly under the control by Thyroid Stimulating Hormone, produced by the master gland, Pitutary Gland. Thyrotropin releasing hormone (TRH) ,produced by Hypothalamus, stimulates the secretion of T3 and T4. The hypothalamic secretion TRH and pituitary secretion of TRH are under negative feedback control of free T4 and free T3.[6]

Thyroid hormone has many effects:

1. Growth
2. Developmental
3. Renal effects

Renal Effects:

- -Increased sodium tubular reabsorption
- -Stimulates renin secretion
- -Control sulfate homeostasis
- -Increase calcium tubular reabsorption.

The first step in thyroid hormone production is uptake of iodide. Then iodide trapping happens by which iodide is actively transported into thyroid cell,where it is "**oxidised**" into iodine. It then combines with tyrosine to produce monoiodotyrosine (MIT) and diiodotyrosine (DIT).

MIT combines with DIT to form T3 whereas combination of two DIT forms T4. Up until secretion thyroid hormones T3 and T4 are in bound form with thyroglobulin. Thyroid peroxidase, the enzyme, catalyzes oxidation, iodination and coupling reactions.

IODIDE--→ ENTERS THYROID CELL---→ IODINE + TYROSINE---→ MIT+DIT

MIT+DIT= T3

DIT +DIT=T4

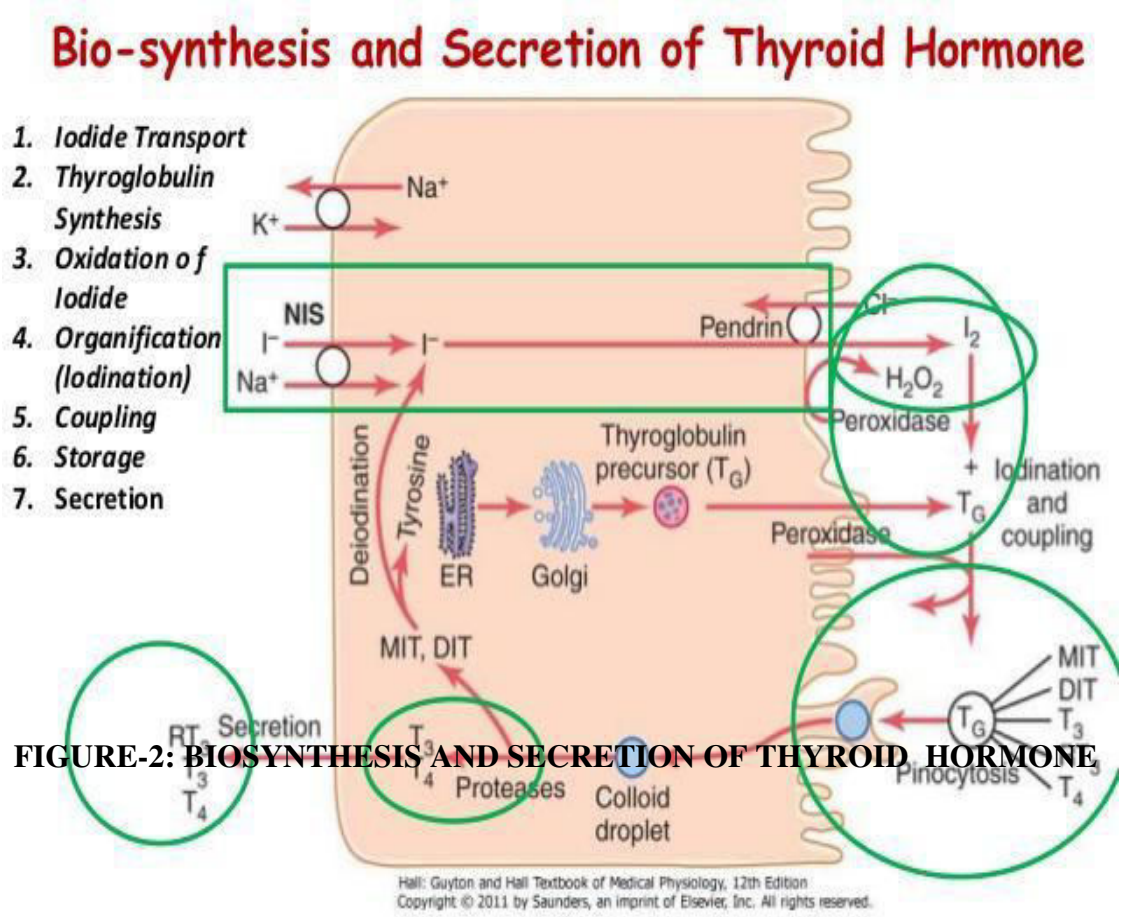


FIGURE-2: BIOSYNTHESIS AND SECRETION OF THYROID HORMONE

Thyroid hormone once secreted into the blood stream , most of T3 and T4 binds with plasma proteins namely, thyroxine – binding globulin and thyroxine – binding prealbumin and albumin. T4 mainly binds with thyroxine – binding globulin whereas T3 binds mainly with albumin. The plasma binding proteins delays hormonal clearance. Increases the circulating availability of hormone, so that it can be delivery to selected tissue sites when if need. The rest of the thyroid hormones are transported in unbound form as free T3 and free T4 .In circulation, there is equilibrium between bound and free form. In peripheral circulation, the enzyme **5' Deiodenase** converts 1/3rd of T4 to T3 and **5 deiodenase** converts 45% of T4 to rT3. Only 13% of T3 is produced and released directly from the thyroid gland, and the remaining 87% is formed from T4.

Half life of T4 is more than that of T3, whereas potency of T3 is more than that of T4. The half life of T4 is seven days and T3 is 10 to 24 hours.

Thyroxine is secreted at a rate of 80 to 90 micrograms/day, tri-iodothyronine at 4 to 5 micrograms/day and reverse T3 is 1 to 2 microgram/day. The plasma level of total T3 is maintained at 0.12 microgram/dl and T4 is 8 microgram/dl.

THYROID AND KIDNEY:

Thyroid hormones plays an important role in renal development and physiology[7,8,9,10,11]. On the other hand kidney disease can lead to thyroid abnormalities.

Effects of thyroid hormone on renal development:

It aids in cell growth and protein synthesis. The functioning renal mass (kidney to body mass ratio) is influenced by thyroid hormone. In hypothyroidism this ratio is reduced and increased in hyperthyroidism in which there is protein breakdown and finally renal atrophy occurs in severe hyperthyroidism.Thyroid hormone causes increased activity of Na-P co-transporter, Na-H exchanger and Na/K ATPase in the proximal convoluted tubule.

Effect of thyroid hormone on renal physiology:

Thyroid hormones affects renal function directly and indirectly. The indirect effect is shown upon cardiovascular system and renal blood flow. The direct effect is that it acts upon on glomerular filtration rate, tubular secretory and reabsorptive function and hormonal influences.

The thyroid hormone favours and increases the activity of Na/K/ATPase in Renal proximal convoluted tubule and also causes increased sodium reabsorption. Thyroid hormones also has effects on tubular potassium permeability[12]and tubular calcium reabsorption[13]. By adrenergic regulation[14], thyroid hormones also influences the renin angiotensin aldosterone(RAAS) axis and influences Renin release[15].

TABLE 4. EFFECT OF THYROID DYSFUNCTION ON THE KIDNEY

	Hypothyroidism	**Hyperthyroidism**
Glomerular filtration	Decreased	Increased
Serum creatinine	Increased	Decreased
Renal plasma flow	Decreased	Increased
Sodium reabsorption	Decreased	Increased

Hypothyroidism and Renal function

In hypothyroidism features like increased serum creatinine level [4],decreased glomerular filtration(GFR) and renal plasma flow are there. By the direct effect of thyroid hormone on cardiovascular system , there is rise in peripheral vascular resistance, poor myocardial contractility and stroke volume and its effect on metabolism leads to hyperlipidemia. The indirect effects of thyroid hormones happen through insulin like growth factor type I and vascular endothelial growth factor

The most frequent electrolyte abnormality seen in hypothyroidism is hyponatremia.(Decreased Serum Sodium). It is predominantly due to decreased GFR, producing reduced water delivery to distal tubules in kidney. The other possible cause being inappropriate ADH secretion .The proximal tubular reabsorption of sodium ,water and chloride are decreased. The microscopic changes such as glomerular basement membrane thickening and mesangial matrix expansion are frequently noticed in hypothyroidism, which causes decremental renal blood flow. The sensitivity of collecting duct to vasopressin receptor is regulated inversely, thus causing increased free water reabsorption. There is reduced production of Cystatin –C, so that serum levels of Cystatin – C is subnormal in hypothyroidism. Treatment of hypothyroidism with levothyroxine could reverse most of the above mentioned changes.

Hyperthyroidism and renal function

Thyroid hormones have positive chronotrophic (Heart Rate)[16], inotrophic[17] effect(Contractility) and also reduced systemic vascular resistance,[18] which indirectly leads to increased renal blood flow.

The other indirect effects of thyroid hormones to increase blood flow to kidney are by raised endothelial making of nitric oxide[19] along with decreasing production of endothelin, a potent renal vasoconstrictor.

In hyperthyroidism, GFR is raised by about 18 – 25%[56], this is due to raised renal blood flow. There is also increased beta adrenergic activity and more positive stimulation of renin angiotensin aldosterone system due to hyperthyroidism. The increased renin angiotensin aldosterone activity causes afferent arteriolar vasodilatation and efferent arteriolar vasoconstriction which consequently produces increased glomerular filtration rate (GFR).

In hyperthyroidism, there is stimulated activity of apical Na-H exchanger, basolateral Na/K/ ATPase, Na – Pi co-transporter.

In hyperthyroidism, serum creatinine is proportionately reduced due to increased glomerular filtration(GFR) and fall in overall muscle mass[61]. Due to glomerular hyperfiltration, there is a raise in 24 hour – urinary protein excretion.

CKD and thyroid function abnormalities

Hyperthyroidism favours progression of CKD by various mechanisms which includes,

- It causes intraglomerular hypertension which produces increased filtration pressure and consequent raised filtration.
- It predisposes to proteinuria which may cause direct renal injury.
- Inverse regulation of superoxide dismutase and raised mitochondrial energy metabolism causes more free radical generation and subsequent renal injury.
- Oxidative stress.

One of the earliest thyroid dysfunction seen among chronic kidney disease patients is low level of T3 hormone (particularly total T3 than Free T3).

This is called as low T3 syndrome.

Low T3 syndrome occurs in CKD because of

- Persistent metabolic acidosis
- Fasting state
- Protein malnutrition
- Decresed peripheral conversion of T4 to T3
- Iodothyronine deiodination

The inflammatory cytokines like tumor necrosis factor alpha (TNF alpha) interleukin – 1 (IL -1) .In CKD, patient inhibits the expression' of enzyme type 1,5 deiodinase, which is required for peripheral conversion of T4 to T3.

There is raised serum iodine level due to dysfunctional renal handling, Leading to Wolff – Chaikoff effect.

There is decreased iodide excretion resulting in raised serum iodide level and iodine content of thyroid gland which sebsequently produces enlargement of thyroid gland. There is more prevalence of Goitre, thyroid nodule, thyroid carcinoma in chronic kidney disease patients when compared to general population.

The CKD mediated thyroid function abnormalities are reversible after renal transplantation. Within the first three to four months of Renal Transplantation low T3 and low T4 level are reversed.

Other renal diseases associated with thyroid dysfunction

- Membranous nephropathy[20,21].
- Minimal change disease[22].
- Ig A nephropathy[23].
- Membranous proliferative glomerular nephritis[24].
- Tubulointerstitial nephritis and uveitis[25].

DIAGNOSIS OF PRIMARY THYROID DISEASES

Recent studies have shown that there is more prevalence of hypothyroidism in chronic kidney disease. Since several symptoms of both hypothyroidism and chronic kidney disease are similar in clinical picture, there is considerable difficulty in differentiating both conditions on clinical background alone. So, all the CKD patients with symptoms suggestive of hypothyroidism should be routed to hypothyroidism screening.

The diagnosis of hypothyroidism should be made only if the following criteria exist:

- There should be a elevated basal TSH value of > 20 μIU/m1.
- Dual total and free T4 level should be distinctly low in the presence of normal TBG.
- Existence of anti thyroid antibodies can provide clue for hypothyroidism.

Reverse T3 is not very useful because it is reduced in CKD.

In CKD, primary hyperthyroidism is exceedingly rare. This condition should be diagnosed with,

- Raised serum total and free T4 concentration.
- Reduced serum TSH values.

High serum T4 level with low T3 in the presence of CKD should make the presence of T4 thyrotoxicosis. This is due to suppression of serum T3 level in low T3 syndrome but serum T4 remains unaffected.

MANAGEMENT

There are sample studies which have been done in patients with the Low T3 syndrome in order to manage and correct the thyroid profile by admionitration of Levothyroxine and Triiodothyronine

Gregory Brent et al[26] conducted a study in non thyroidal illness patients. They managed all the patients with serum total T4 less than 5 tg/dl with 1.5 mcg/Kg of levothyroxine for upto 2 weeks. There is significant raise in thyroxine level in treated patients.

There is also significant surge in serum T3 levels. Unfortunately, increased mortality was seen in the treatment group on day 5-17.

Carter et al studied effects of administration of Triiodothyronine in the patients with CKD. The study stated that there is no change in serum T3 level over a period of 3 months. The mean serum T4 and TSH levels were altered significantly. But there was no subjective improvement appreciated in this group of patients.

Based on the fore-mentioned observations, it has been suggested that low serum T3 level in patients with CKD has its metabolically protective effect and it is interpreted as a functional adaptation to a reduced basal metabolic rate (BMR) and to preserve energy in an adverse environment. Because of that, this condition has been renamed as “Thyroid hormone adaptation syndrome”.

There is decreased TSH level and increased catabolism, seen on administration with T4 or T3. Hence, giving thyroid hormone is non-beneficial in patients with CKD. The study also shows that there is raised in mortality with the treatment. So, thyroid hormone replacement should be avoided in CKD patients unless true hypothyroidism is evident.

PROGNOSIS

The magnitude of the thyroid dysfuncion that occurs in patients fulfilling the criteria for chronic kidney disease(CKD), in general shows the severity of the illness. The prognosis is poor in patients with low levels of serum T3 and T4 or TSH concentration. Studies have stated that there is reversal thyroid function abnormalities in CKD patients post renal transplantation.

3.4 DYSLIPIDEMIAS

The population and studies have shown that total and low-density lipoprotein (LDL)-cholesterol values are two of the most important independent predictors of cardiovascular morbidity and mortality [27] Factors contributing to elevated triglycerides in the general population include: obesity, physical inactivity, cigarette smoking, excess alcohol intake, type 2 diabetes, chronic renal failure, and estrogen

ATP III Classification of Total, LDL and HDL Cholesterol(mg/dL)

Total Cholesterol

<200mg/dL	Desirable
200-239mg/dL	Borderline high
>240mg/dL	High

LDL Cholesterol

<100mg/dL	Optimal
100-129mg/dL	above optimal
130-159mg/dL	Borderline high
160-189mg/dL	High
>190mg/dL	Very high

HDL Cholesterol

<40mg/dL	Low
>60mg/dL	High

Triglycerides

<150 mg/dL	Normal triglycerides
150-199 mg/dL	Borderline-high
200-499mg/dl	High
>500 mg/dL	very high

Pathways of Lipid Transport

Two pathways of lipid transport are:

Exogenous Pathway

Dietary triglycerides are hydrolyzed within the intestinal lumen and emulsified with bile acids to form micelles. Cholesterol is esterified in the enterocyte to form cholesteryl esters . Nascent chylomicrons are secreted into the intestinal lymph and delivered via the thoracic duct. The particles encounter lipoprotein lipase (LPL).The triglycerides are hydrolyzed by LPL, and free fatty acids are released. The released free fatty acids are taken up by adjacent myocytes or adipocytes and either oxidized to generate energy or stored as triglyceride. The chylomicron progressively shrinks in size creating chylomicron remnants, which are rapidly removed from the circulation by the liver.

Endogenous Pathway

The triglycerides of VLDL are derived from the esterification of long-chain fatty acids. The packaging of hepatic triglycerides with the components of the nascent VLDL particle (apoB-100, cholesteryl esters, phospholipids and vitamin E, requires the action of the enzyme microsomal triglyceride transfer protein (MTP).After secretion into the plasma, VLDL acquires multiple copies of apoE and apolipoproteins of the C series. As with chylomicrons, the triglycerides of VLDL are hydrolyzed by LPL. After

the VLDL remnants dissociate from LPL contain roughly similar amounts of cholesterol and triglyceride. The liver removes approximately 40–60% of IDL by LDL receptor–mediated endocytosis via binding to apoE .*Lipoprotein(a)* [Lp(a)] .

Apo(a) is synthesized in the liver and attached to apoB-100.The major site of clearance of Lp(a) is the liver.

HDL Metabolism

Cholesterol in peripheral cells is transported from peripheral cells to the liver and intestine by a process termed "reverse cholesterol transport" ,facilitated by HDL.

HDL cholesterol is transported to hepatocytes by an indirect and a direct pathway. HDL cholesteryl esters can be transferred to apoB-containing lipoproteins in exchange for triglyceride CETP. The cholesteryl esters are then removed by LDL receptor–mediated endocytosis. HDL cholesterol can also be taken up directly by hepatocytes via the scavenger receptor class B1 (SR-B1).

CKD and Dyslipidemia

It varies according to renal function and degree of proteinuria. As GFR falls TGL increase and as proteinuria increases TC,TGL,LDL increases.

Low HDL is an independent risk factor for CKD events. [28]

According to ARIC(Atherosclerosis risk in communities) Study High TGL and low HDL increases the risk of CKD. [29]

Dyslipidemia, regardless of underlying cause (DM, HT), has a role in progression of CKD.[30]

According to ATP (Adult Treatment program) III , in the management of CKD focuses on LDL as an important target.[31]

Sharma, *et al* [32] and Kunde et al [33] observed no hyperlipidemia in patients of CRF.

Whereas, Gupta [34] and Das *et al* [35] observed Hypertriglyceridemia and reduced High density lipoprotein (HDL).

Triglyceride levels

Hypertriglyceridemia is partially due to down regulation of lipoprotein lipase (LPL), hepatic lipase, VLDL and low-density lipoprotein receptor (LDL-r) expression [36] and also increased plasma apoC-III and apoC-II. [37]

The down regulation of expression of several genes [38-40] along with the changes in the composition of lipoprotein particles [41] represent the most important pathophysiological mechanisms behind the development of hypertriglyceridemia in CKD.

CKD-induced hyperparathyroidism to the pathogenesis of lipoprotein lipase deficiency contribute to diminished production and impaired activity

of lipoprotein lipase. Recurrent heparinization in the course of haemodialysis procedure is thought to further contribute to lipoprotein lipase depletion in ESRD patients.[42]

CKD and HDL Abnormalities:

The overall reduction in plasma HDL in the ESRD population which is due to its diminished production [43]. Serum LCAT activity and concentration are highly reduced in CKD patient[44] due to of reduced production by the liver.[45,46]

Also, hypoalbuminemia commonly seen in advanced CKD, may contribute to reduced HDL cholesterol level.

Reduction in HDL cholesterol in CKD is associated with elevated HDL triglyceride. This is due to deficiency in hepatic triglyceride lipase. The reduction in HDL antioxidant is most likely due to the prevailing Oxidative stress .

LDL

Elevated plasma LDL cholesterol concentration not a typical feature of patients with advanced CKD. The proportions of sdLDL and IDL, are increased which are athyerogenic. sdLDL is a subtype of LDL, that has high propensity to penetrate the vessel wall, and triggers the atherosclerotic process. LDL removed from the circulation mainly by macrophages. This leads to formation of cholesterol-laden foam cells, an important step in atheromatous plaque formation Expression of both scavenger receptors, SR-A and CD36, is increased in an uremic patient.Also, uptake of unmodified LDL by LDL receptors is enhanced in inflammation. This also leads to foam cell formation and constitutes a risk factor for atherogenesis.

Total cholesterol

Plasma total cholesterol is usually normal or reduced in patients with ESRD.

Heavy proteinuria leads to up regulation of HMG-CoA reductase Therefore, heavy proteinuria, when present, can modify HMG-CoA reductase expression causing hypercholesterolemia in ESRD patients .

However, heavy proteinuria results in acquired LDL receptor deficiency, which plays a central role in the genesis of hypercholesterolemia.[47,48]

Lipoprotein [Lp(a)]

Lipoprotein [Lp(a)] is an LDL-like particle whose protein moiety contains apolipoprotein (a) [apo(a)]. Lp(a) concentrations are genetically determined by the apo(a) gene. Individuals with high molecular weight have on average low plasma Lp(a) concentrations.

In kidney disease, plasma Lp(a) levels are influenced by GFR. In patients with large apo(a) isoforms plasma Lp(a) levels begin to increase in stage 1 CKD before GFR starts to decrease.[49] In contrast, in patients with nephrotic syndrome increase in plasma Lp(a) levels occur in all apo(a) isoform groups. The elevation of Lp(a) in CKD is an acquired abnormality, mostly influenced by the degree of proteinuria.

It has been shown that Lp(a) is an independent risk factor for CKD population. Its levels are increase in CKD and especially in patients undergoing PD.

DYSLIPIDEMIA – CONSEQUENCES:

Hyperlipidemia can accelerate progression of renal disease by varied mechanisms. Firstly, reabsorption of fatty acids, phospholipids, and cholesterol by tubular epithelial cells can stimulate tubulointerstitial inflammation and tissue injury Secondly, accumulation of lipoproteins in glomerular mesangium can promote matrix production and

glomerulosclerosis[49,50]. And also, impaired HDL-mediated reverse cholesterol transport can further contribute to tissue injury.

Accumulation of oxidation-prone atherogenic lipoproteins and defective HDL-mediated reverse cholesterol transport, which are the important features of uremic dyslipidemia, play a big role in the pathogenesis of atherosclerosis .

MATERIALAS AND METHODS

4. MATERIALS AND METHODS:

A prospective cross sectional study will be conducted among the CKD patients admitted in the dept. of General Medicine, Tirunelveli Medical college & Hospital.

- The subjects are selected based on the inclusion and exclusion criteria.
- The details of the patient are obtained in the pre-set proforma after getting informed consent in the regional language.
- Routine laboratory investigations,Thyroid function tests and Lipid profile will be done.

Analysis shall be made using SPSS software.

Inclusion criteria:

Patients admitted in Dept. of Medicine ,Tirunelveli Medical College hospital and diagnosed as Chronic kidney disease patients.

Exclusion criteria:

- Known cases of thyroid dysfunction
- Known cases of dyslipidemia
- Patients undergoing dialysis
- Pregnant women

Study site :

Dept. of General Medicine, Tirunelveli Medical College hospital, Tirunelveli.

Sample size : 100 patients

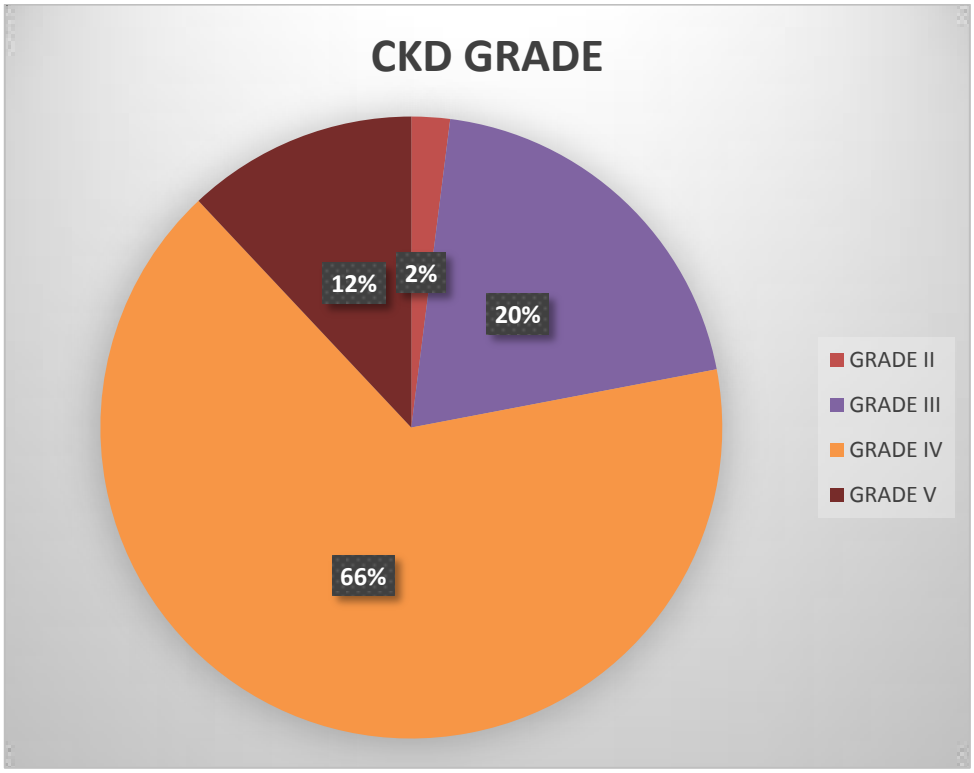
Study duration: 1 year

RESULTS AND ANALYSIS

5. RESULTS AND ANALYSIS

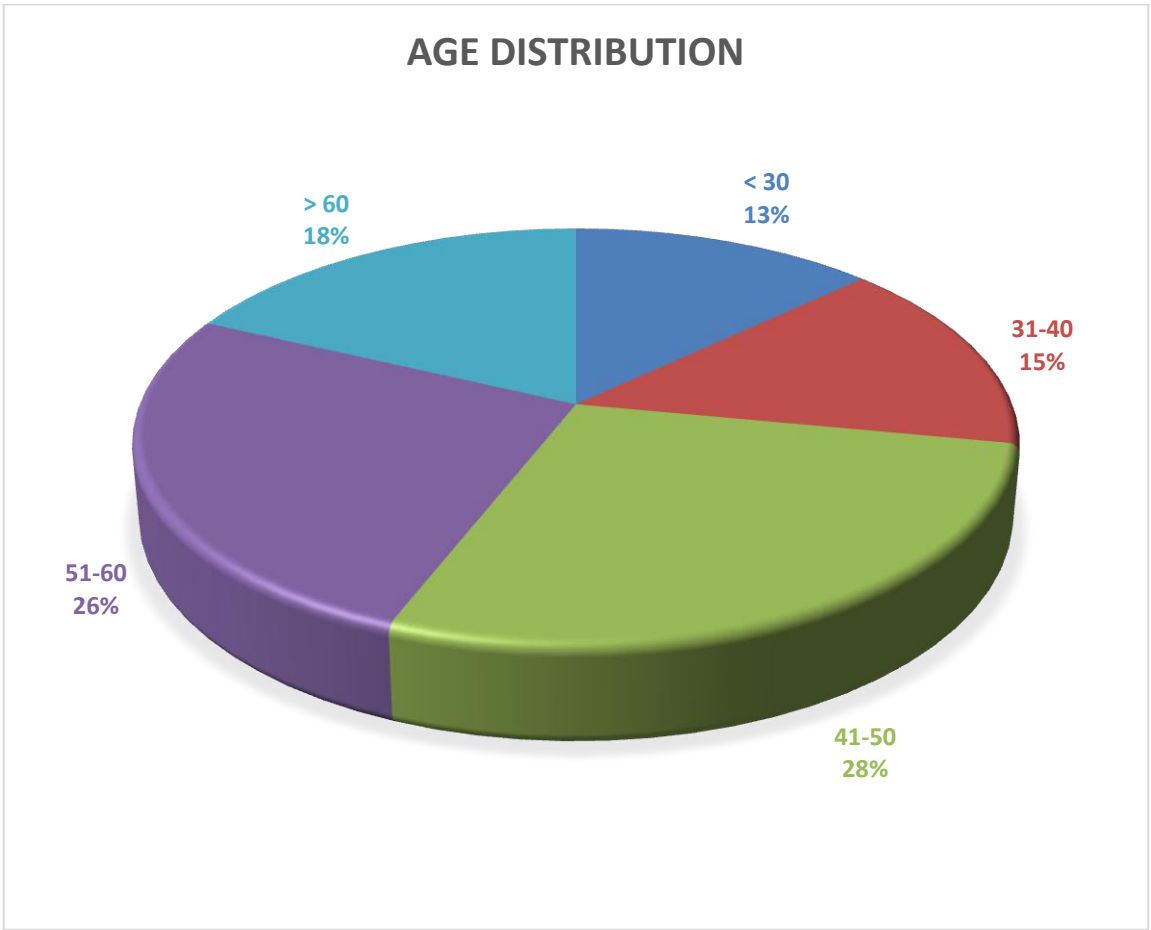
5.1 CKD GRADE IN STUDY POPULATION:

CKD GRADE	NO OF PATIENTS	PERCENTAGE
GRADE II	2	2%
GRADE III	20	20%
GRADE IV	66	66%
GRADE V	12	12%



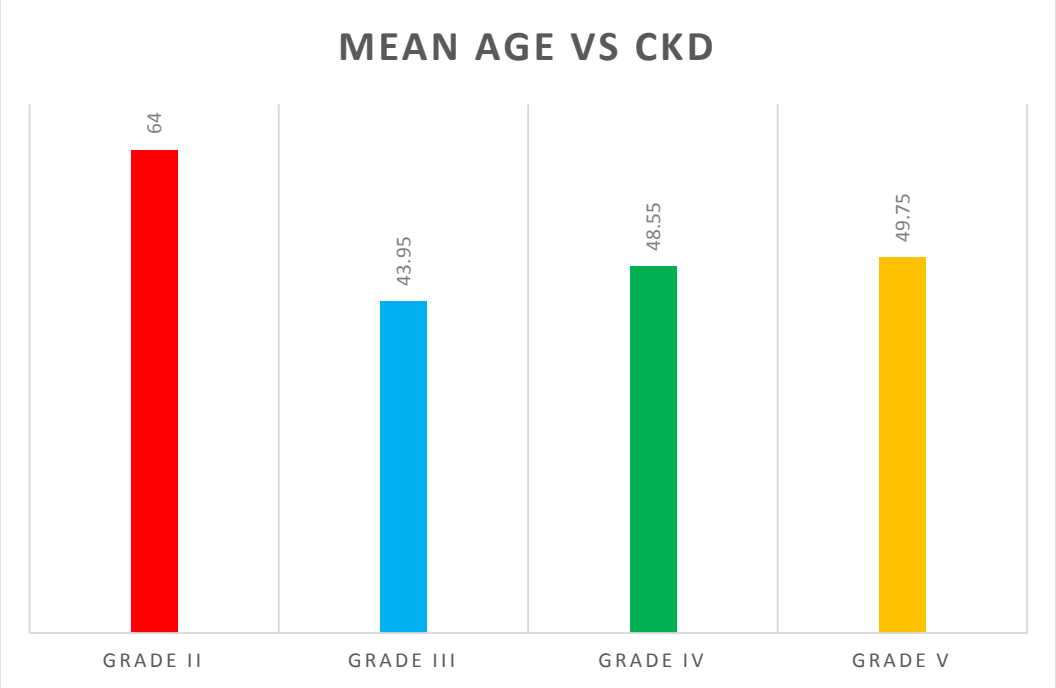
5.2 AGE DISTRIBUTION

AGE IN YEARS	NO OF PATIENTS	PERCENTAGE
< 30	13	13%
31-40	15	15%
41-50	28	28%
51-60	26	26%
> 60	18	18%



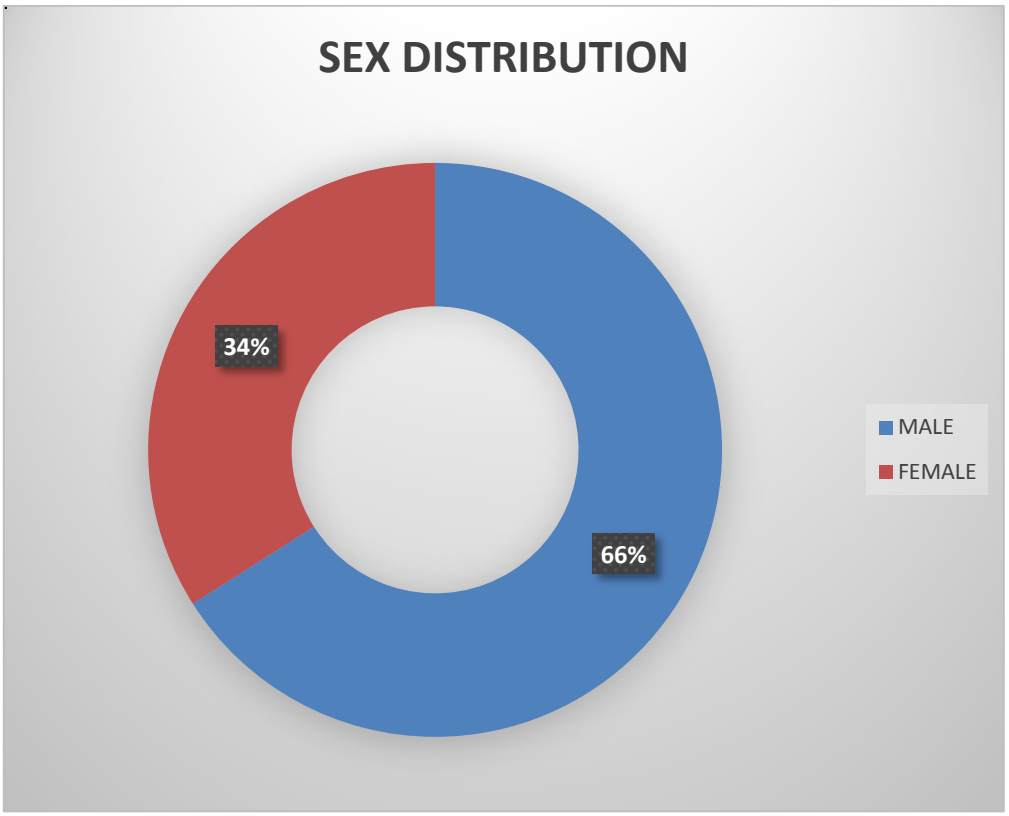
5.3 DISTRIBUTION OF MEAN AGE VS CKD:

CKD GRADE	AGE IN YEARS	
	MEAN	SD
GRADE II	64	5.65
GRADE III	43.95	14.35
GRADE IV	48.55	13.94
GRADE V	49.75	10.21
ANOVA		
P VALUE - 0.179		
NON SIGNIFICANT		



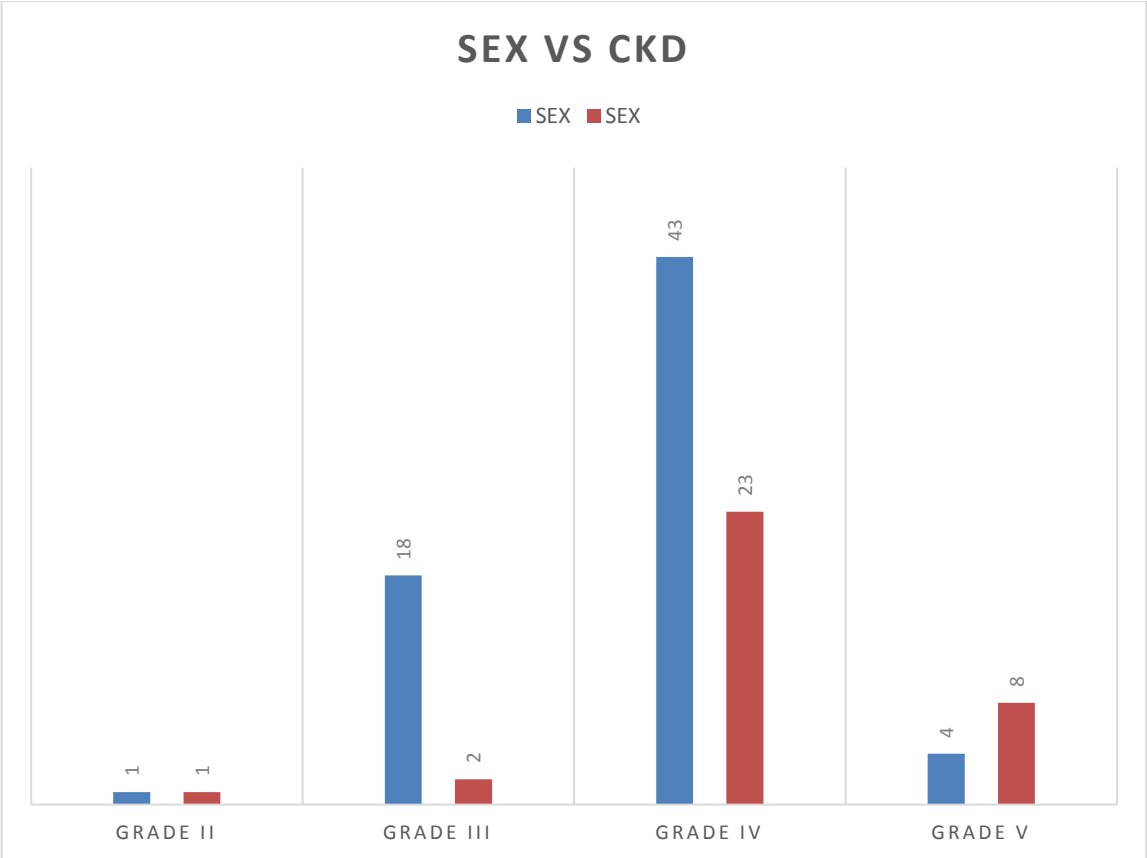
5.4 CKD PREVALENCE IN MALE AND FEMALE:

SEX	NO OF PATIENTS	PERCENTAGE
MALE	66	66%
FEMALE	34	34%



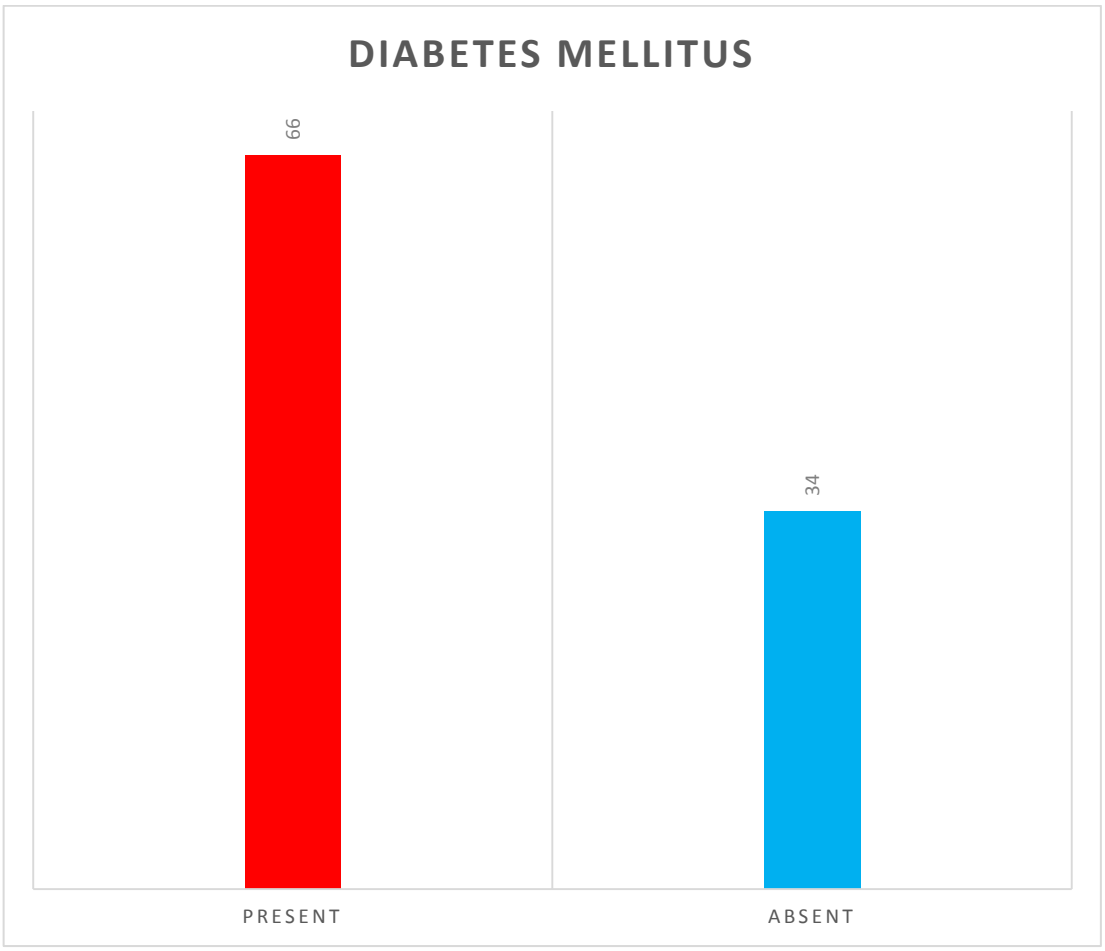
5.5 SEX DISTRIBUTION IN VARIOUS GRADES OF CKD:

CKD GRADE	SEX	
	MALE	FEMALE
GRADE II	1	1
GRADE III	18	2
GRADE IV	43	23
GRADE V	4	8



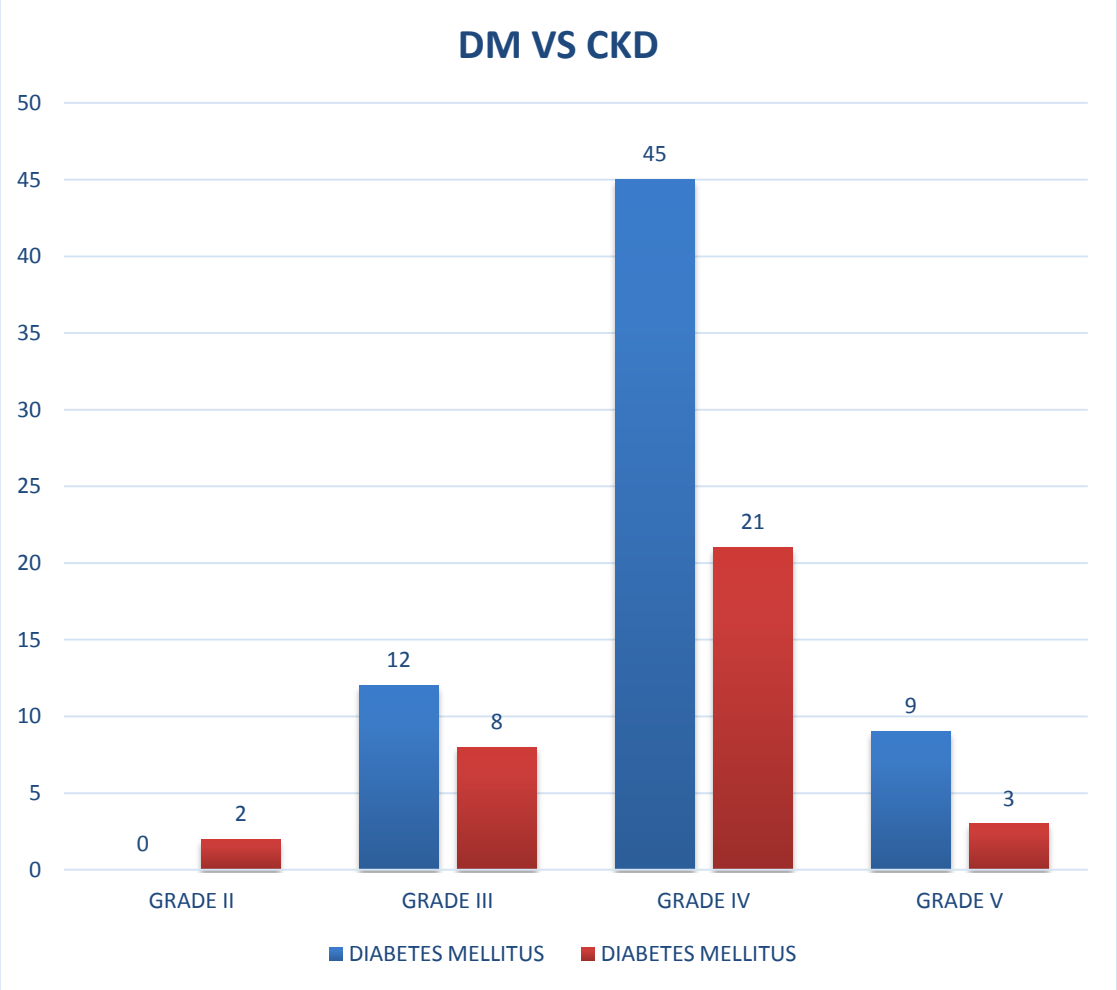
5.6 PREVALENCE OF DIABETES MELLITUS IN CKD:

DIABETES MELLITUS	NO OF PATIENTS	PERCENTAGE
PRESENT	66	66%
ABSENT	34	34%



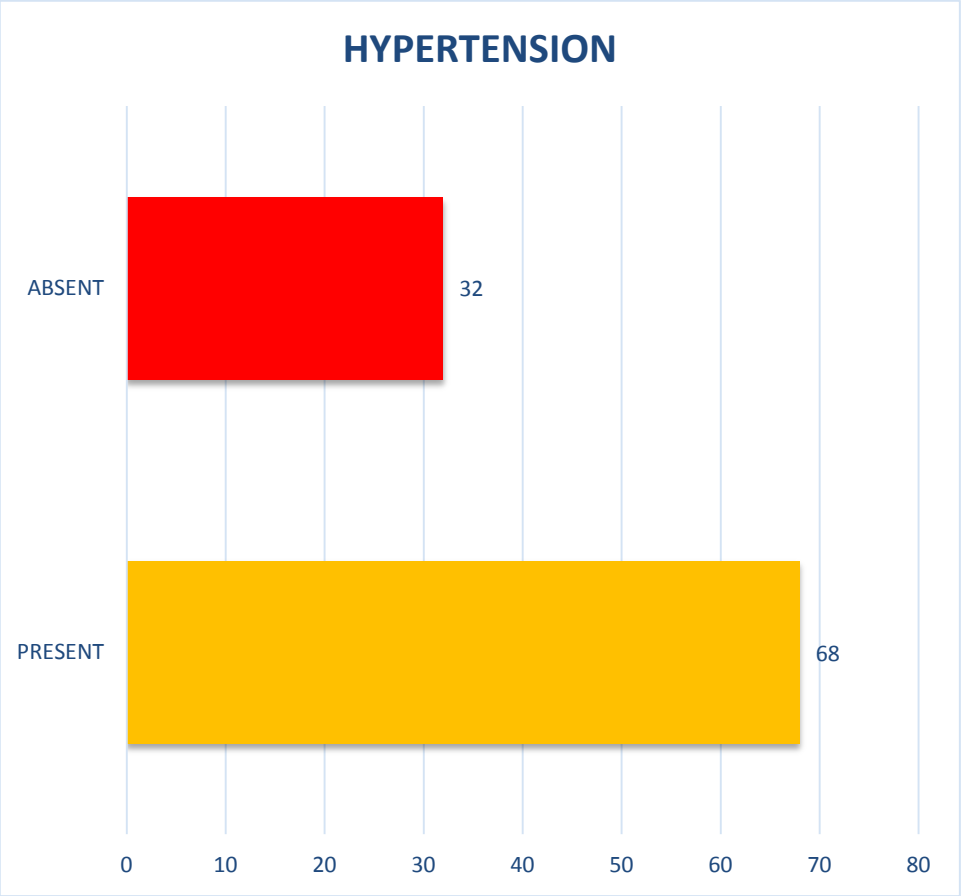
5.7 PREVALENCE OF DIABETES MELLITUS IN VARIOUS GRADES OF CKD:

CKD GRADE	DIABETES MELLITUS	
	PRESENT	ABSENT
GRADE II	0	2
GRADE III	12	8
GRADE IV	45	21
GRADE V	9	3



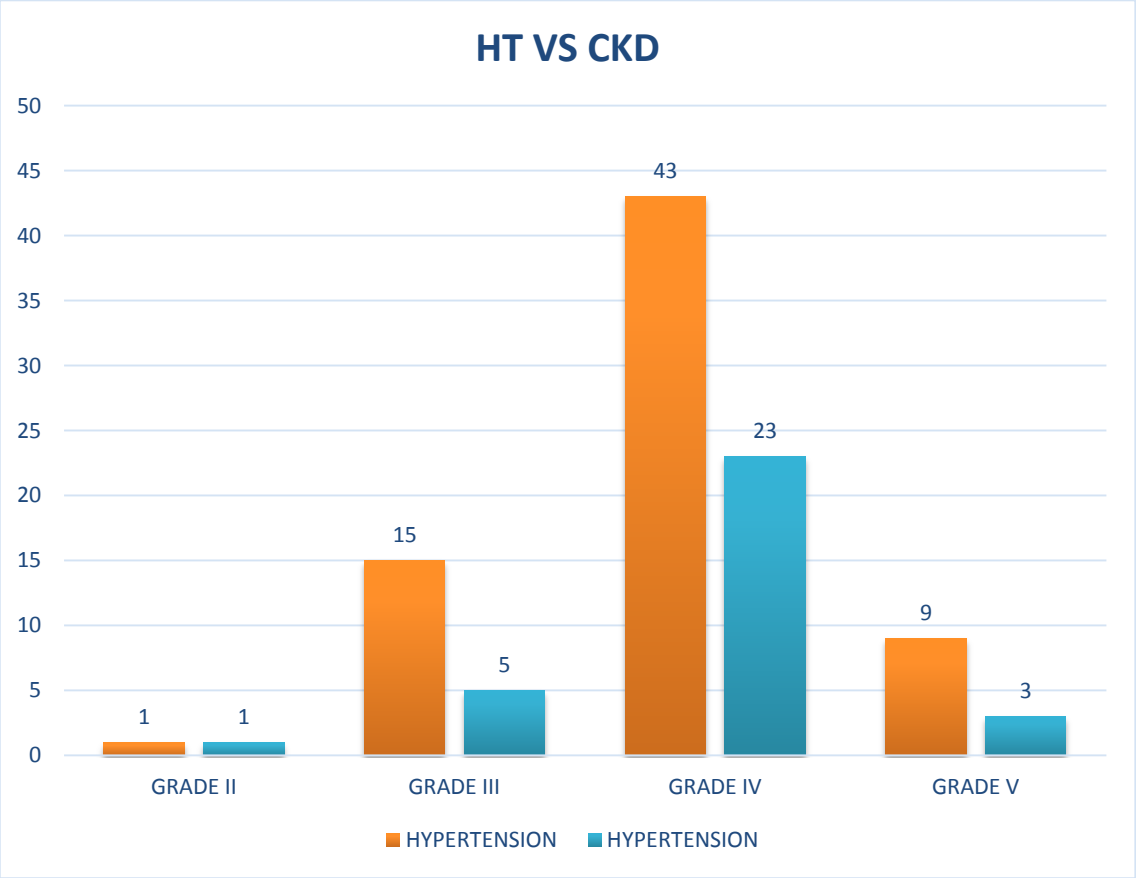
5.8 PREVALENCE OF HYPERTENSION IN CKD:

HYPERTENSION	NO OF PATIENTS	PERCENTAGE
PRESENT	68	68%
ABSENT	32	32%



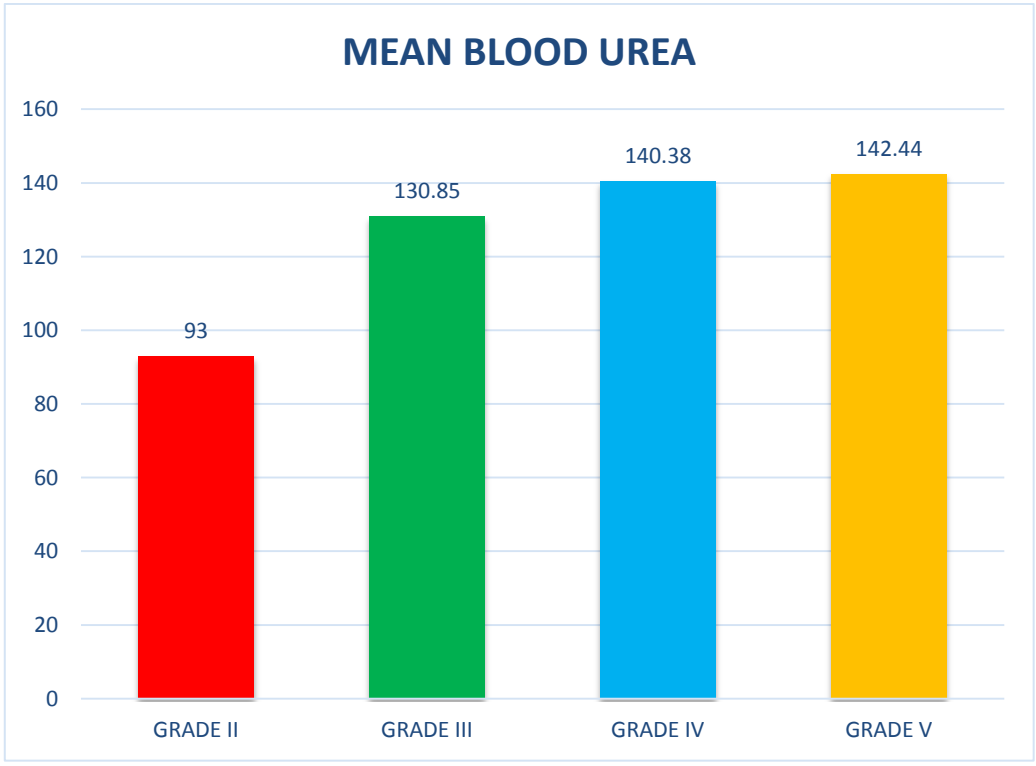
5.9 PREVALENCE OF HYPERTENSION IN VARIOUS GRADES OF CKD:

CKD GRADE	HYPERTENSION	
	PRESENT	ABSENT
GRADE II	1	1
GRADE III	15	5
GRADE IV	43	23
GRADE V	9	3



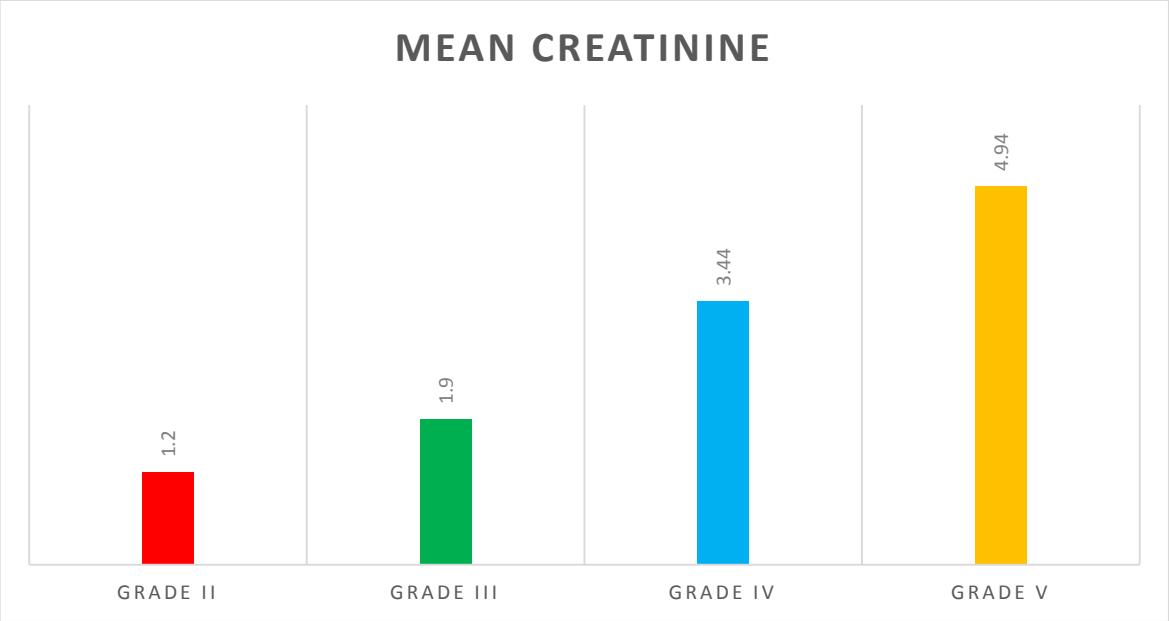
5.10 DISTRIBUTION OF BLOOD UREA IN CHRONIC KIDNEY DISEASE:

CKD GRADE	BLOOD UREA	
	MEAN	SD
GRADE II	93	12.72
GRADE III	130.85	69.74
GRADE IV	140.38	40.04
GRADE V	142.44	25.6
ANOVA		
P VALUE - 0.505		
NON SIGNIFICANT		



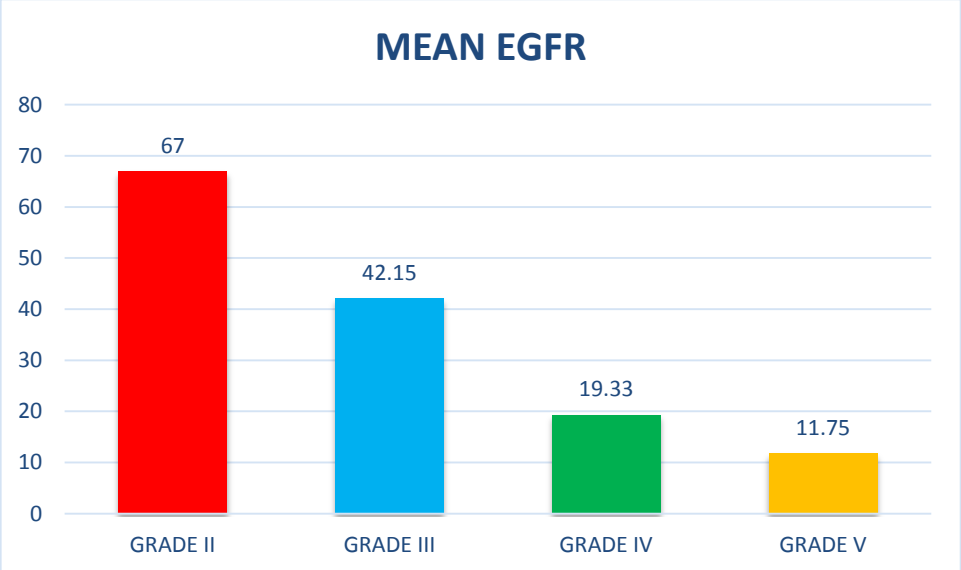
5.11 DISTRIBUTION OF SERUM CREATININE IN CHRONIC KIDNEY DISEASE:

CKD GRADE	SERUM CREATININE	
	MEAN	SD
GRADE II	1.2	0
GRADE III	1.9	0.3
GRADE IV	3.44	0.69
GRADE V	4.94	1.75
ANOVA		
P VALUE - 0.001		
SIGNIFICANT		



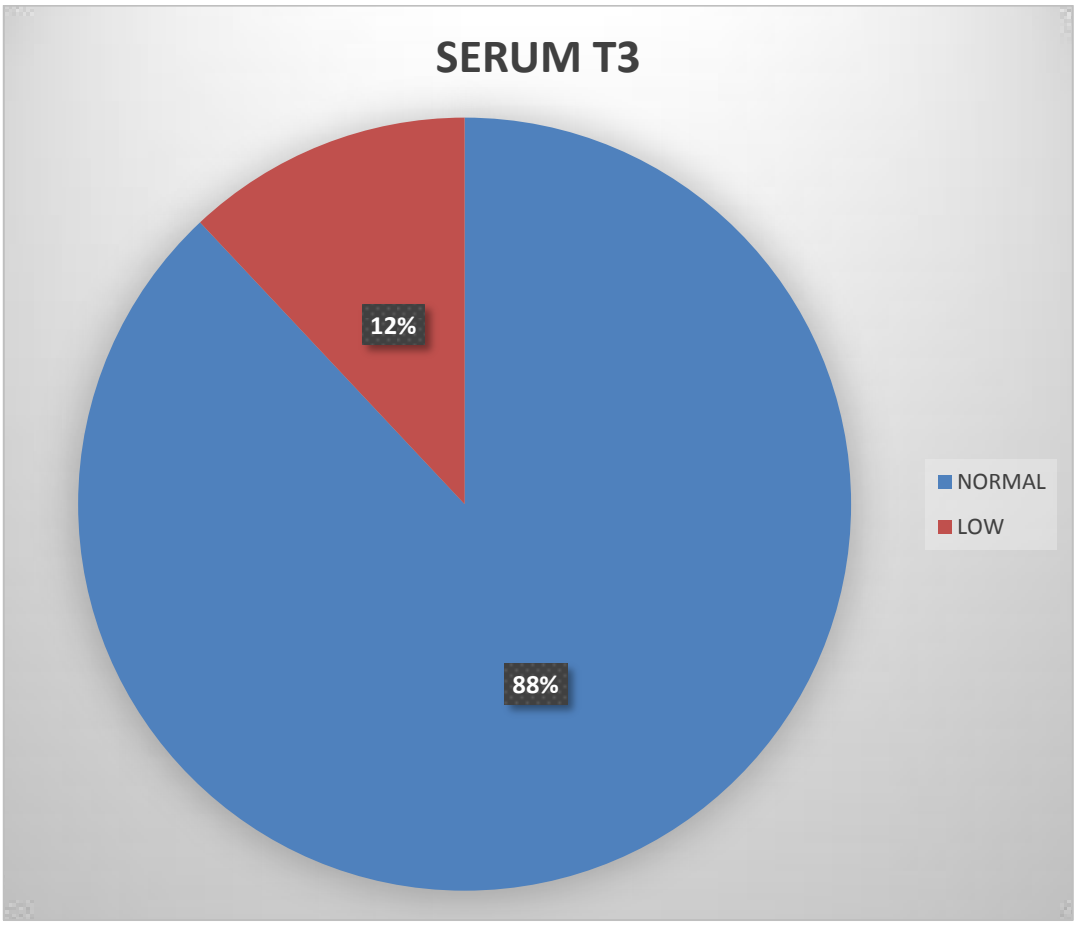
5.12 DISTRIBUTION OF EGFR IN VARIOUS GRADES OF CHRONIC KIDNEY DISEASE:

CKD GRADE	EGFR	
	MEAN	SD
GRADE II	67	1.41
GRADE III	42.15	8.49
GRADE IV	19.33	3.84
GRADE V	11.75	2.41
ANOVA		
P VALUE - 0.001		
NON SIGNIFICANT		



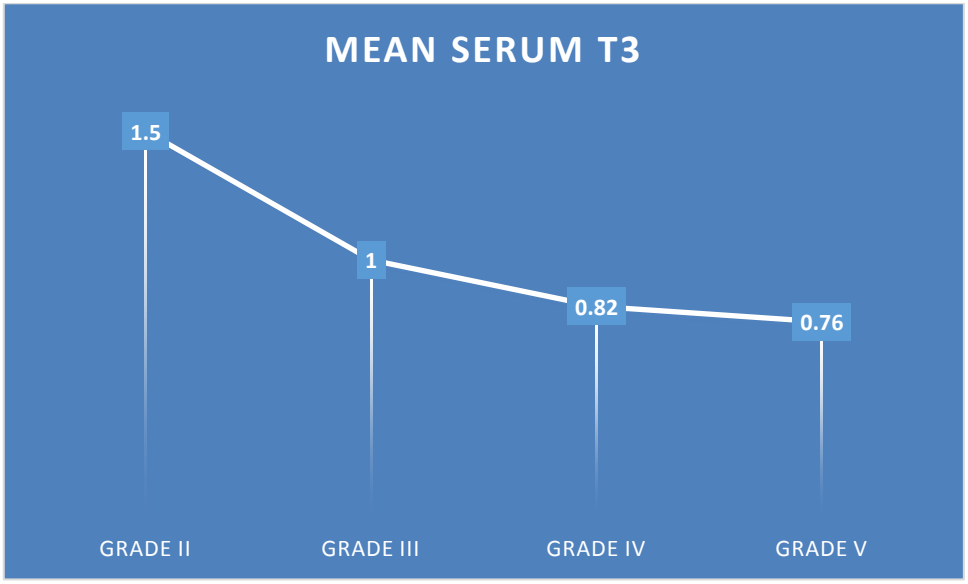
5.13 DISTRIBUTION OF SERUM T3 LEVELS IN STUDY POPULATION:

SERUM T3	NO OF PATIENTS	PERCENTAGE
NORMAL	88	88%
LOW	12	12%



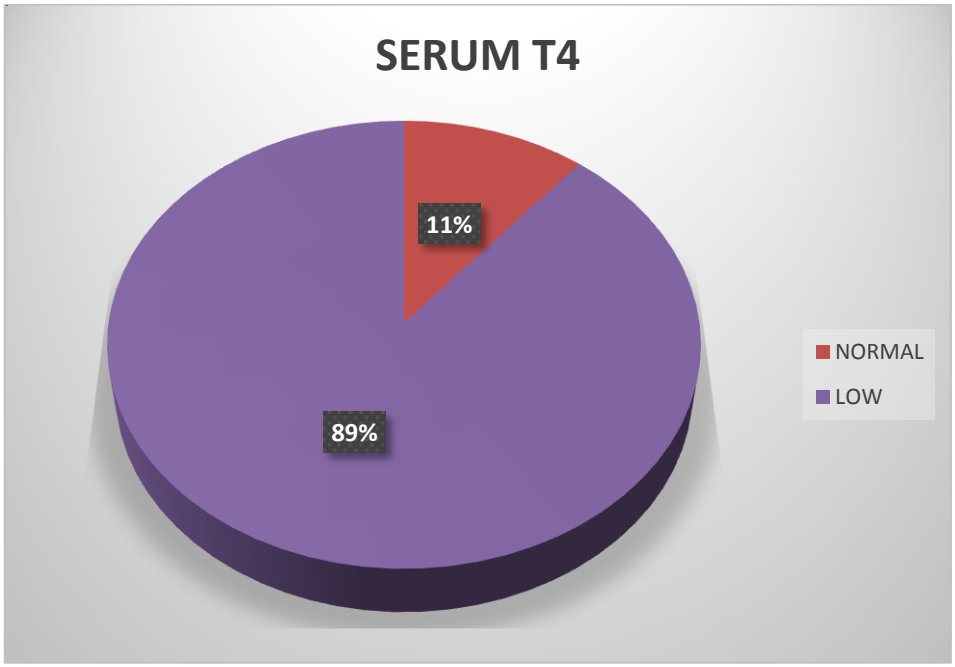
5.14 DISTRIBUTION OF SERUM T3 LEVELS IN CHRONIC KIDNEY DISEASE:

CKD GRADE	SERUM T3	
	MEAN	SD
GRADE II	1.5	0.14
GRADE III	1	0.26
GRADE IV	0.82	0.34
GRADE V	0.76	0.29
ANOVA		
P VALUE - 0.001		
SIGNIFICANT		



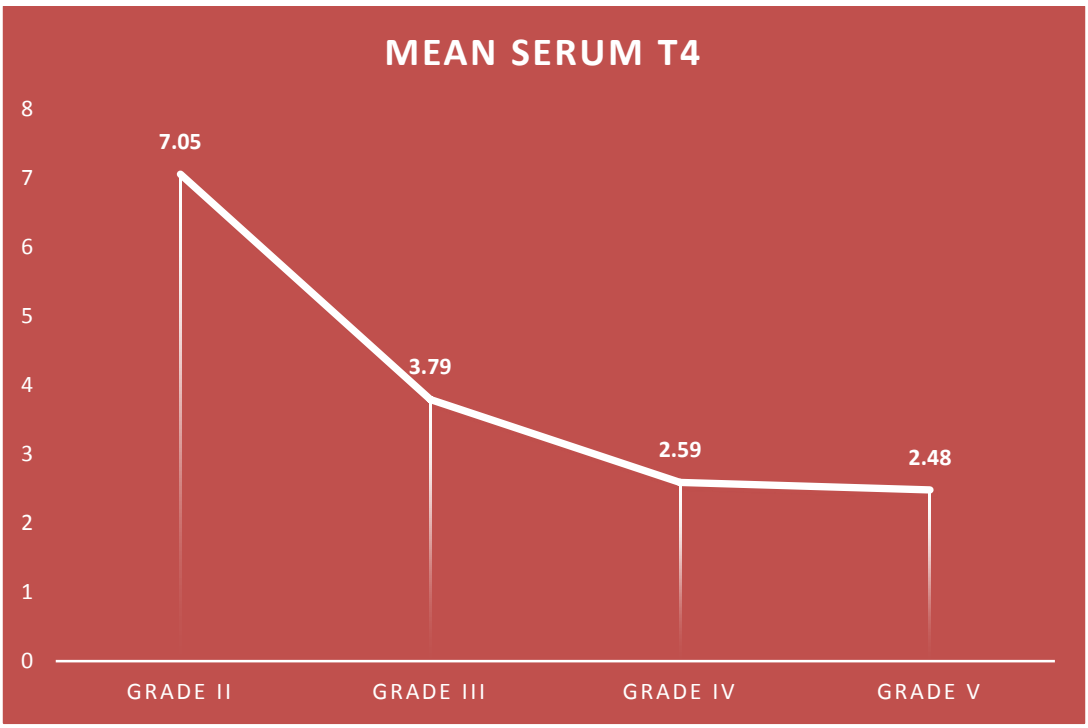
5.15 DISTRIBUTION OF SERUM T4 LEVELS IN CHRONIC KIDNEY DISEASE:

SERUM T4	NO OF PATIENTS	PERCENTAGE
NORMAL	11	11%
LOW	89	89%



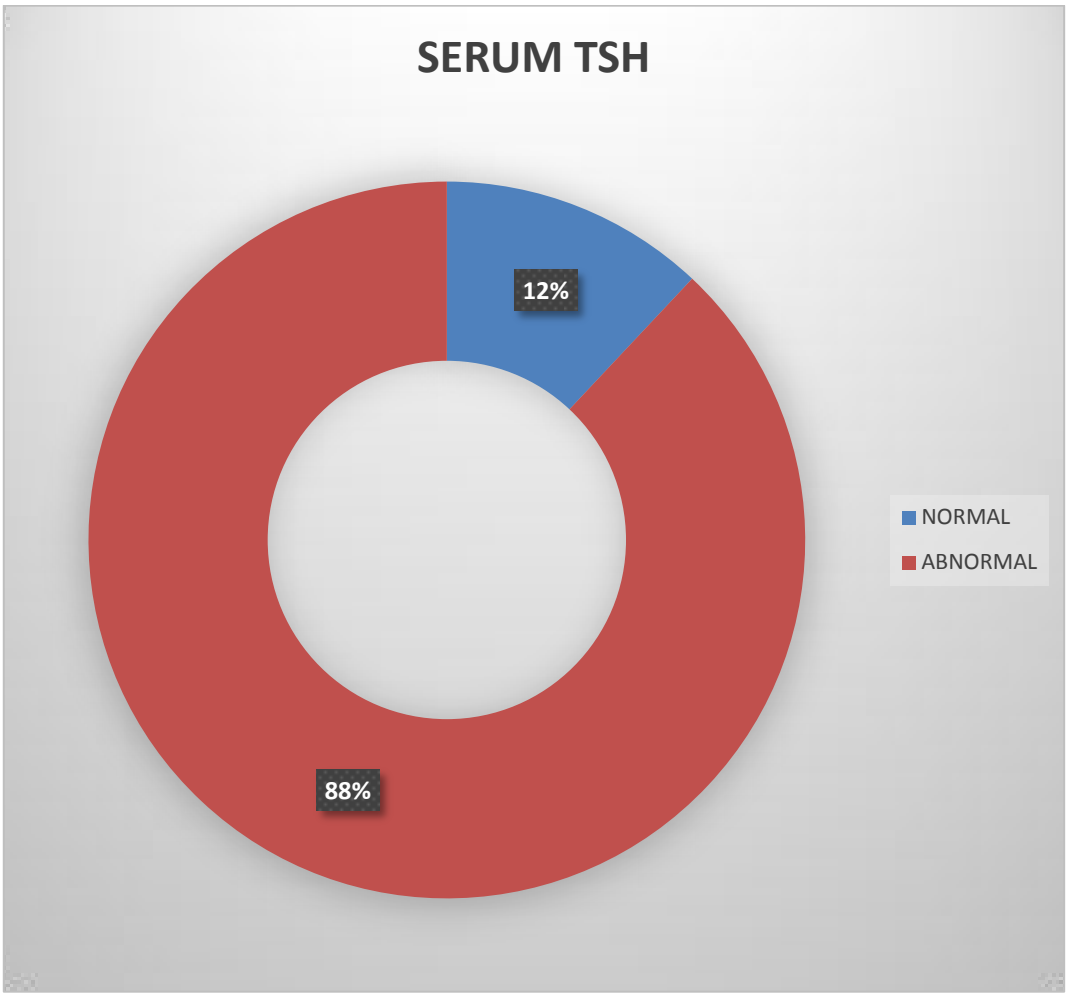
5.16 DISTRIBUTION OF SERUM T3 LEVELS IN VARIOUS GRADES OF CHRONIC KIDNEY DISEASE:

CKD GRADE	SERUM T4	
	MEAN	SD
GRADE II	7.05	0.77
GRADE III	3.79	0.72
GRADE IV	2.59	1.07
GRADE V	2.48	0.99
ANOVA		
P VALUE - 0.006		
SIGNIFICANT		



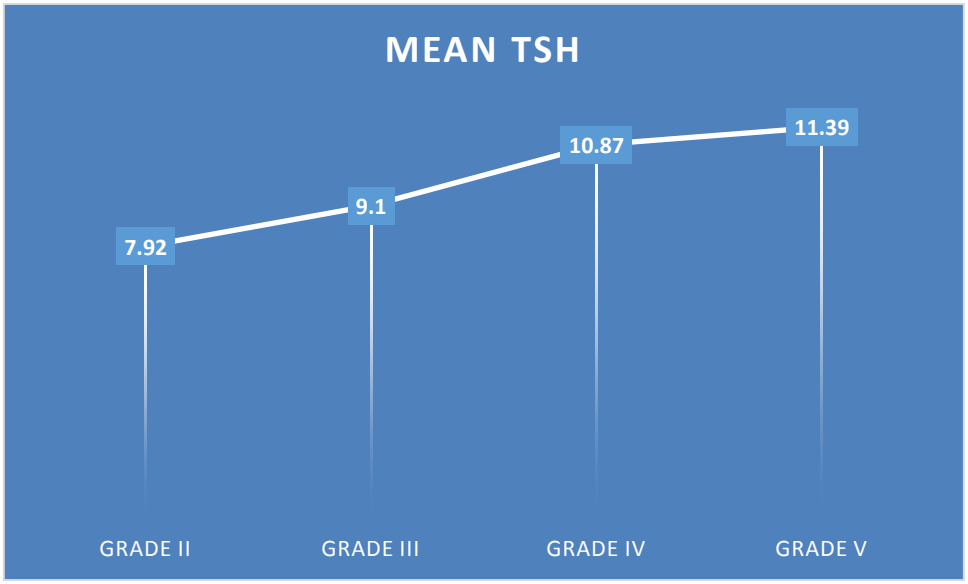
5.17 DISTRIBUTION OF SERUM TSH LEVELS IN CHRONIC KIDNEY DISEASE:

SERUM TSH	NO OF PATIENTS	PERCENTAGE
NORMAL	12	12%
ABNORMAL	88	88%



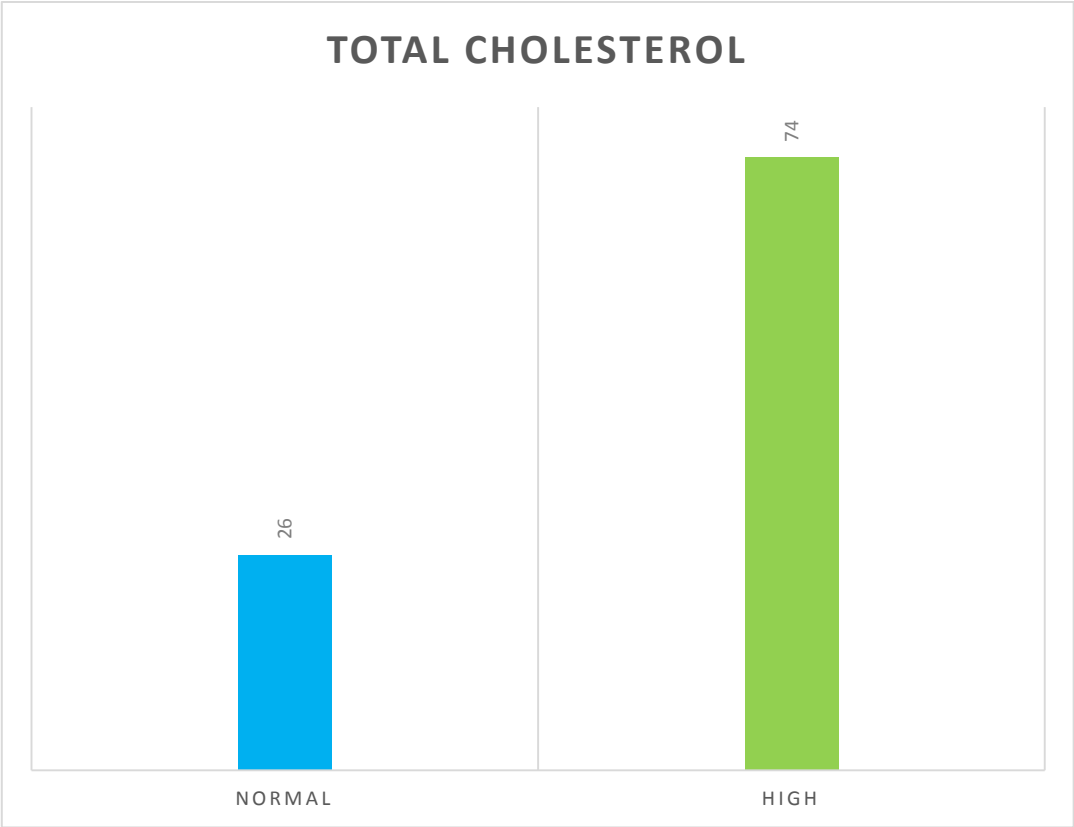
5.18 DISTRIBUTION OF SERUM TSH LEVELS IN VARIOUS GRADES OF CHRONIC KIDNEY DISEASE:

CKD GRADE	SERUM TSH	
	MEAN	SD
GRADE II	7.92	0.59
GRADE III	9.1	2.78
GRADE IV	10.87	2.45
GRADE V	11.39	2.17
ANOVA		
P VALUE - 0.001		
SIGNIFICANT		



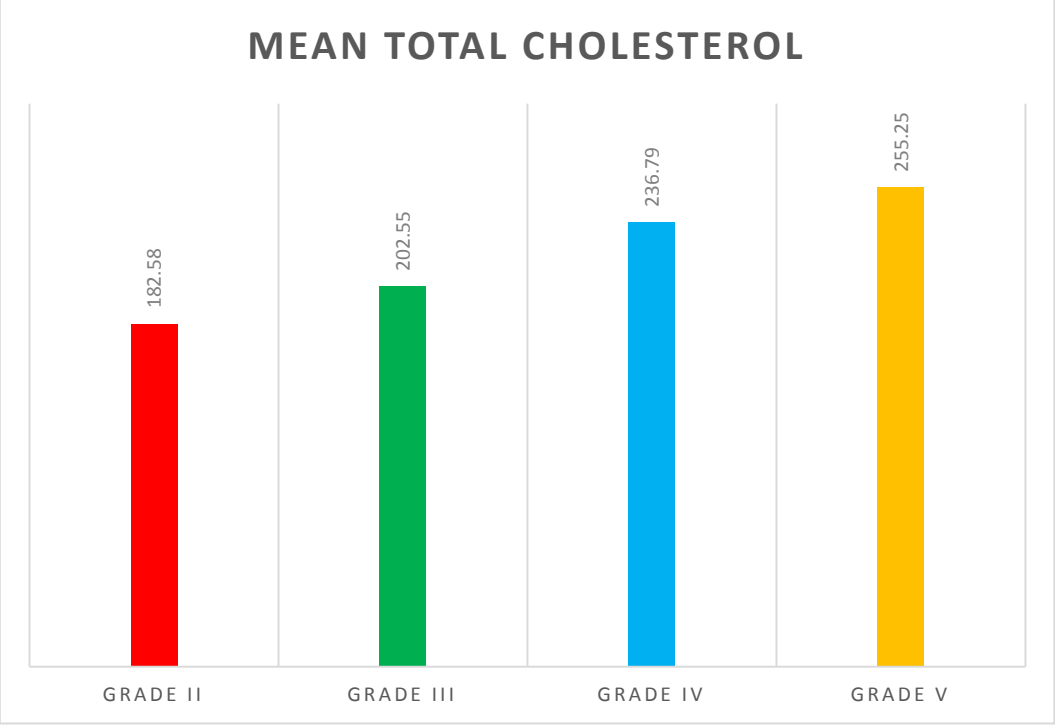
5.19 DISTRIBUTION OF TOTAL CHOLESTEROL LEVELS IN CHRONIC KIDNEY DISEASE:

TOTAL CHOLESTEROL	NO OF PATIENTS	PERCENTAGE
NORMAL	26	26%
HIGH	74	74%



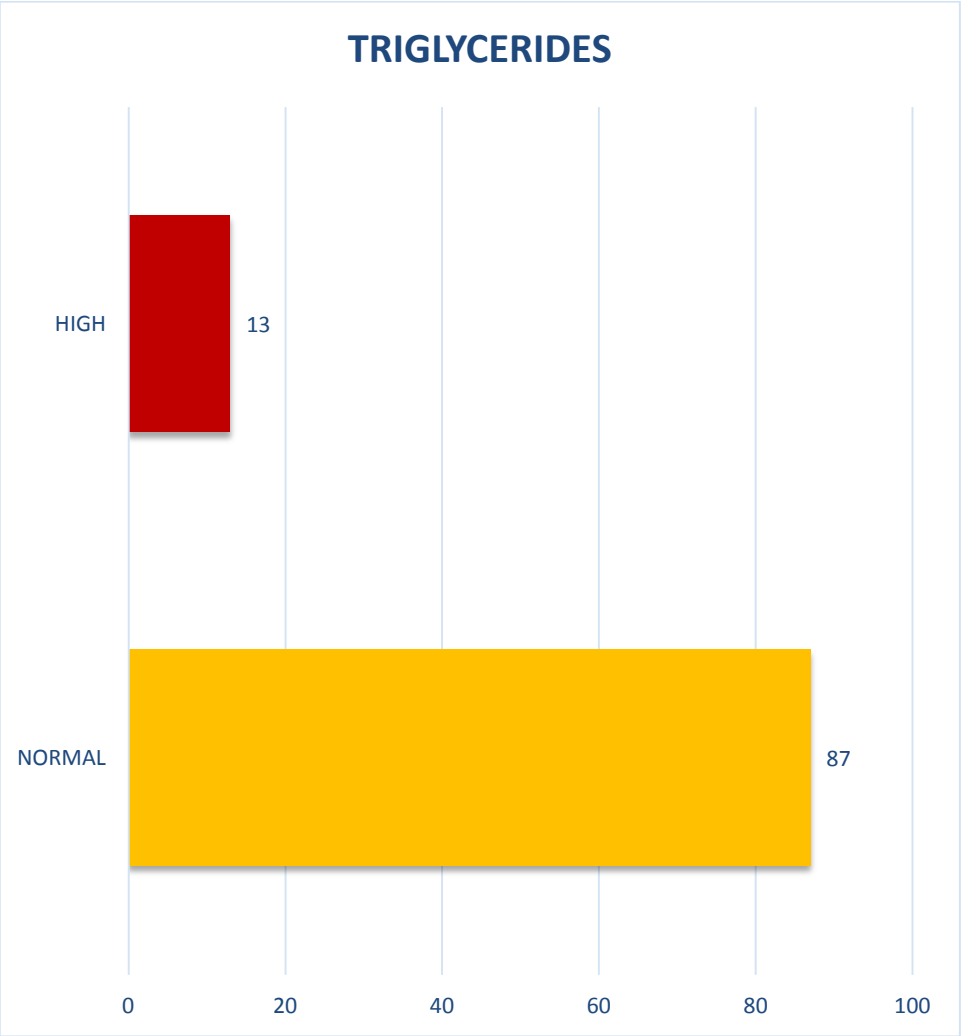
5.20 DISTRIBUTION OF TOTAL CHOLESTEROL LEVELS IN VARIOUS GRADES OF CHRONIC KIDNEY DISEASE

CKD GRADE	TOTAL CHOLESTEROL	
	MEAN	SD
GRADE II	182.58	17.67
GRADE III	202.55	19.28
GRADE IV	236.79	35.96
GRADE V	255.25	34.94
ANOVA		
P VALUE - 0.001		
SIGNIFICANT		



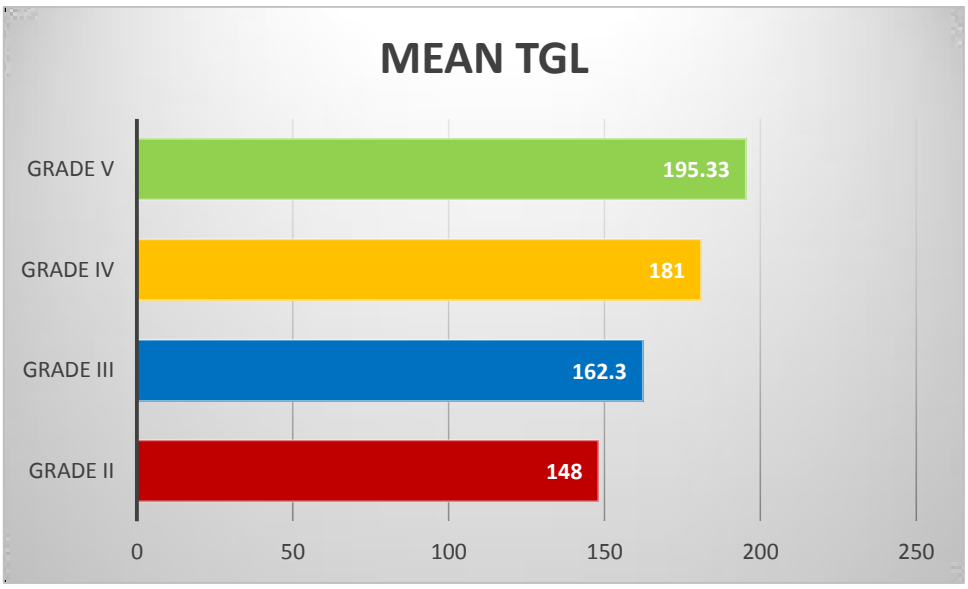
5.21 DISTRIBUTION OF TRIGLYCERIDES LEVELS IN CHRONIC KIDNEY DISEASE

TRIGLYCERIDES	NO OF PATIENTS	PERCENTAGE
NORMAL	87	87%
HIGH	13	13%



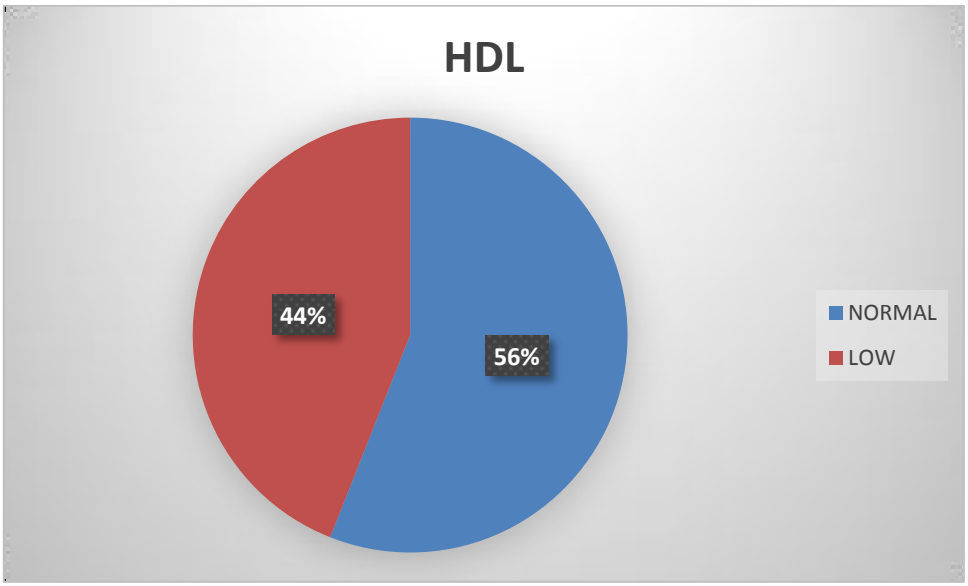
5.22 DISTRIBUTION OF TRIGLYCERIDES LEVELS IN VARIOUS GRADES OF CHRONIC KIDNEY DISEASE

CKD GRADE	TRIGLYCERIDES	
	MEAN	SD
GRADE II	148	5.65
GRADE III	162.3	32.79
GRADE IV	181	52.99
GRADE V	195.33	13.32
ANOVA		
P VALUE - 0.171		
NON SIGNIFICANT		



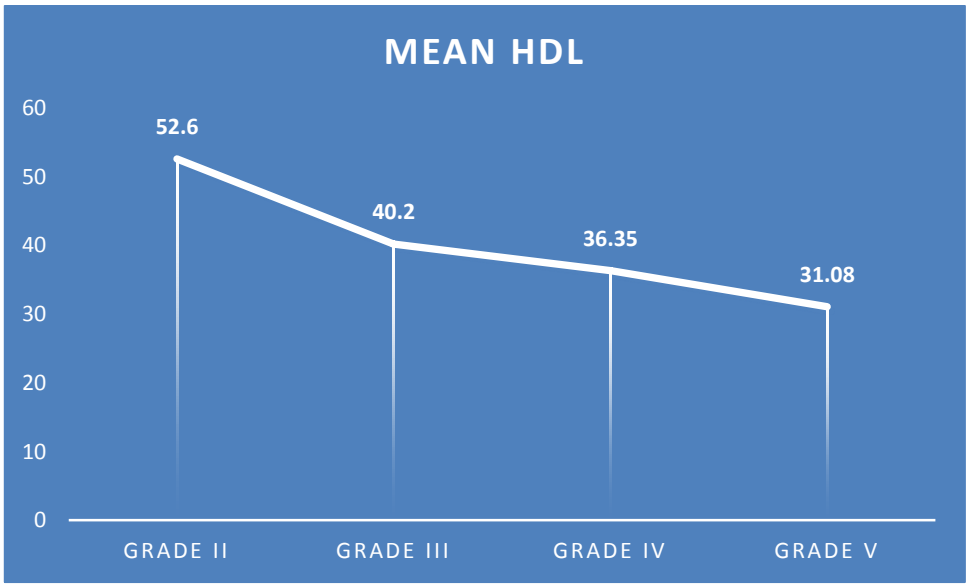
5.23 DISTRIBUTION OF HIGH DENSITY LIPOPROTEINS LEVELS IN CHRONIC KIDNEY DISEASE

HDL	NO OF PATIENTS	PERCENTAGE
NORMAL	56	56%
LOW	44	44%



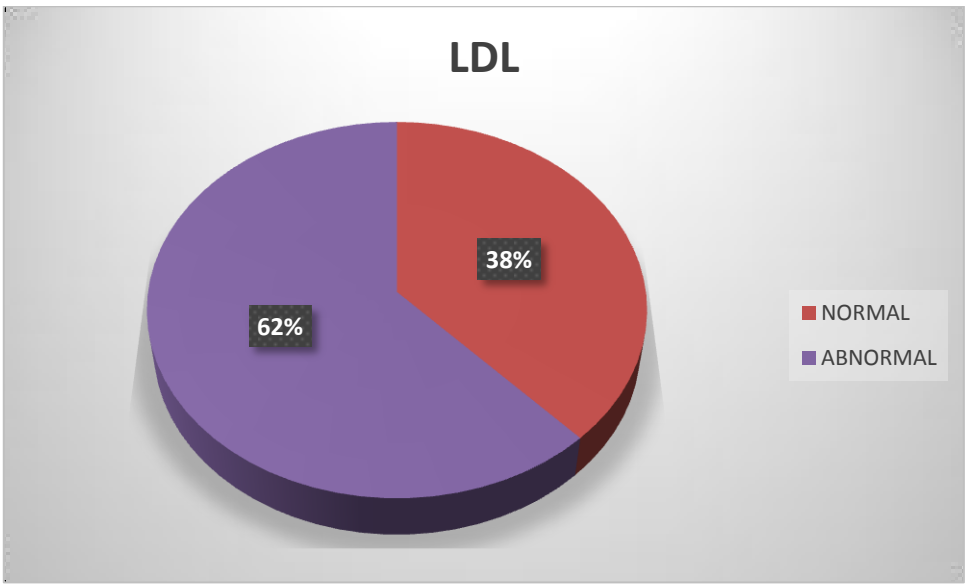
5.24 DISTRIBUTION OF HIGH DENSITY LIPOPROTEINS LEVELS IN VARIOUS LEVELS OF CHRONIC KIDNEY DISEASE

CKD GRADE	HIGH DENSITY LIPOPROTEIN	
	MEAN	SD
GRADE II	52.6	5.65
GRADE III	40.2	10.79
GRADE IV	36.35	3.18
GRADE V	31.08	3.47
ANOVA		
P VALUE - 0.001		
SIGNIFICANT		



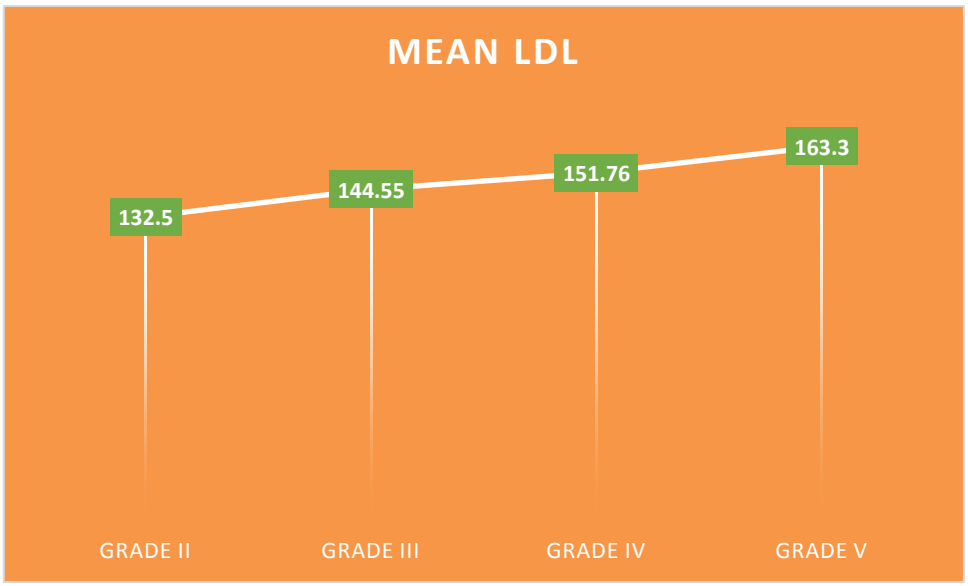
5.25 DISTRIBUTION OF LOW DENSITY LIPOPROTEINS LEVELS IN CHRONIC KIDNEY DISEASE

LDL	NO OF PATIENTS	PERCENTAGE
NORMAL	38	38%
ABNORMAL	62	62%



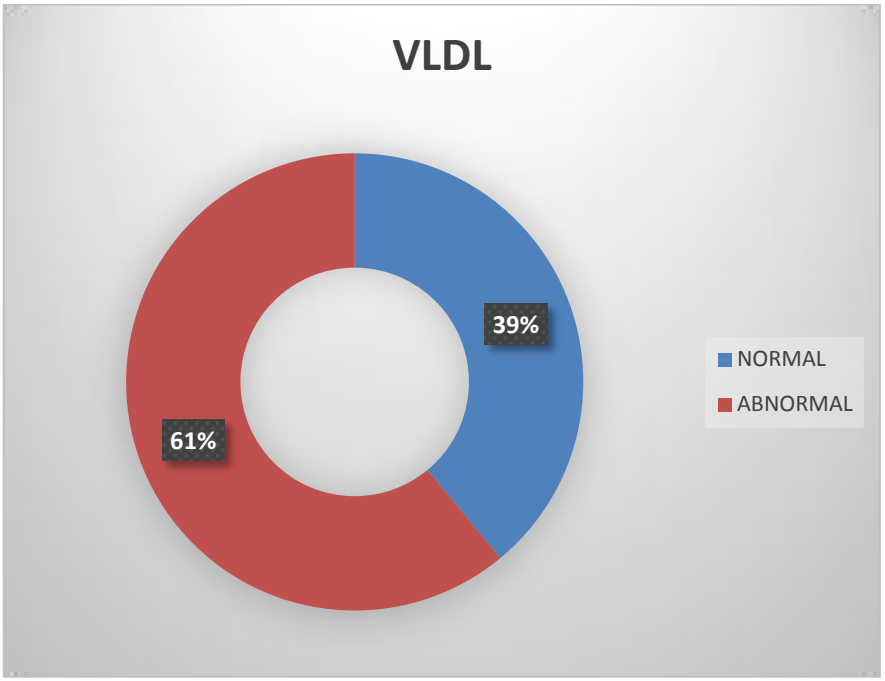
5.26 DISTRIBUTION OF HIGH DENSITY LIPOPROTEINS LEVELS IN VARIOUS GRADES OF CHRONIC KIDNEY DISEASE

CKD GRADE	LOW DENSITY LIPOPROTEIN	
	MEAN	SD
GRADE II	132.5	17.67
GRADE III	144.55	19.76
GRADE IV	151.76	29.04
GRADE V	163.3	22.76
ANOVA		
P VALUE - 0.199		
NON SIGNIFICANT		



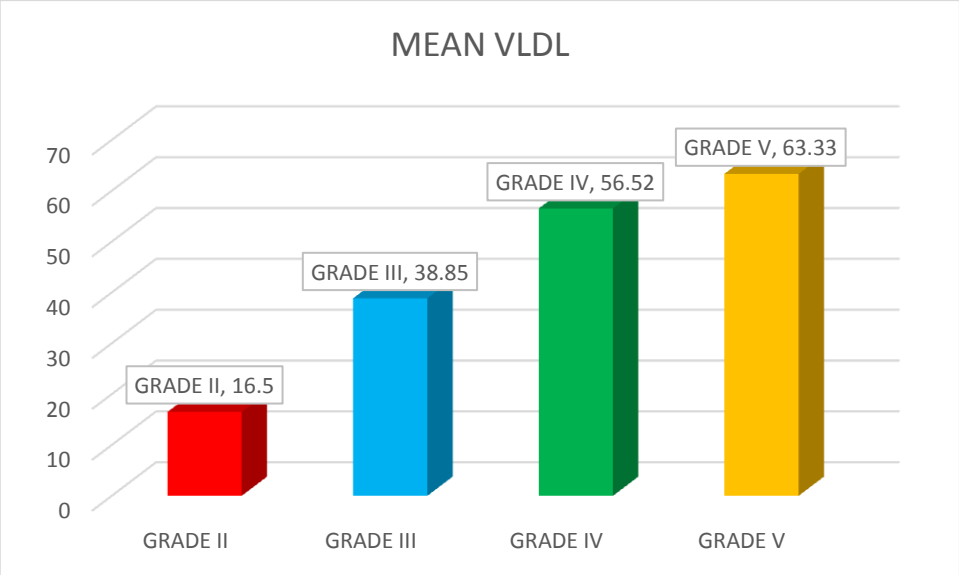
5.27 DISTRIBUTION OF VERY LOW DENSITY LIPOPROTEINS LEVELS IN CHRONIC KIDNEY DISEASE

VLDL	NO OF PATIENTS	PERCENTAGE
NORMAL	39	39%
ABNORMAL	61	61%



5.28 DISTRIBUTION OF VERY LOW DENSITY LIPOPROTEINS LEVELS IN VARIOUS GRADES OF CHRONIC KIDNEY DISEASE

CKD GRADE	VLDL	
	MEAN	SD
GRADE II	16.5	2.12
GRADE III	38.85	8.46
GRADE IV	56.52	17.21
GRADE V	63.33	15.66
ANOVA		
P VALUE - 0.423		
NON SIGNIFICANT		



DISCUSSION

6. DISCUSSION

The motto of the present study was to predict the prevalence of thyroid dysfunction & Lipid abnormalities in CKD patients

To determine the pathological interrelationship between thyroid dysfunction and severity of renal disease, numerous studies were conducted about thyroid function abnormality and severity of CKD and different results have been shown.

In our study, only those CKD patients on conservative line of therapy were studied. This can be attributed to the fact that thyroid profile undergoes changes due to dialysis independent of the presence due to chronic kidney disease. Numerous studies have been studied by comparing CKD patients on conservative line of management and patients on HD by Ramirez[51] and Kayima et al[52].

In our study, 100 patients of CKD, who were on conservative management fulfilling the criteria for CKD were studied, among these 100 patients, 66 were males and 34 were females, their age distribution varied from <30 yrs to >60 years. Among these 100 patients, patients were categorized into <30 yrs, 31-40 yrs, 41-50 yrs, 51-60 yrs,>60yrs.

Among the 100 patients in our study, 66% of patients were males and 34% patients were females.

Of the 100 patients, the mean eGFR ranged from 67ml/min in Stage II CKD to 11.75 ml/min in Stage V CKD in our study.

The blood urea mean value ranged from 93 mg/dl in stage II CKD to 142.44 mg/dl in stage V CKD.

The creatinine mean values varied from 1.2 mg/dl in stage II CKD to 4.9 mg/dl in stage V CKD.

In our study out of 100 patients, 12 patients had low serum T3 levels (12%).

89 patients had low T4 levels in our study (89%).

88 patients had low TSH (88%) and 12 had normal range TSH.

In our study, the decreasing trend in T4 and increasing Trend in TSH showed linear correlation with progressing stages of CKD.

One study done by Spector [53] and Ramirez et al [51] Dudani et al[54], Karunanidhi et al[55]. These studies showed abnormality in hypophyseal mechanism of TSH release in patients with Uraemia as the TSH response to the TRH was reduced.

Another study which was done by Joseph et al and Hardy etal showed up low T3 T4 level with high TSH level indicating maintenance of pituitary thyroid axis. Several studies in CKD patients showed low T3 values. Low T3 had also been reported in Ramirez et al[51], Hegedus et a1, Beckett et al[56]PonAjil Singh et al, P Iglesias and JJ Diez and many others.

Ramirez and Spector et a1[53] study exposed the linear correlation between mean serum T3 and T4 and severity of CKD

Studies by Quionverdeet a1[57] showed high preponderance of hypothyroidism in CKD. It was roughly estimated to be about 5% in patients with final stage of CKD.

Detailed study by Kaptein et al[58] showed the prevalence of primary hypothyroidism was about 2.5 times much higher in chronic kidney disease and dialysis than in normal population. The incidence of hypothyroidism in CKD was estimated to range in between 0 and 9.5%

Kaptein study also calculated the presence of anti thyroid antibody titer in 6.7% of CKD.

The symptoms of hypothyroidism were distributed equally in both hypothyroid and CKD patients in our study.

So, diagnosis of hypothyroidism in CKD more importantly depends on TSH level which must be very high (>20 μIU/dl) with low level of serum T4. In this study, none of the patients had clinical or biochemical features of hyperthyroidism.

As a go with other studies, mean T3 level in our study was decreased in GFR less than 15 ml/min. In patients with reduced GFR, T3 level was found to be reduced and it shows that there was straight line relationship between level of T3,T4 and GFR, which is consistent with Avinashi et al study.

GOITRE:

Study by Ramirez et a1[51] showed high prevalence of goiter in patients with CKD especially those undergoing chronic dialysis. The incidence was found to be raised in end stage renal disease. The possible explanation could be due to accumulation of iodides in Thyroid gland due to reduced renal clearance in CKD patients. Other than goiter, study conducted by Hegedus et al showed the volume of thyroid gland was significantly increased in patients with CKD. In our study, no patient had goitre.

CKD AND LIPID

In our study, most frequent lipid abnormalities documented were low HDL levels and hypercholesterolemia.

DECREASED HIGH DENSITY LIPOPROTEIN LEVELS

In our study, 56 out of 100 patients with CKD had low levels of HDL.

The low HDL levels in patients with chronic kidney disease in our study were in match with Diana M Lee LG et al [59] who studied the abnormalities of lipid profile in CRF patients.

This low HDL cholesterol levels was also an isolated independent risk factor for the development of CKD in the Framingham spring study. Several pathological processes may underlie the reductions in HDL cholesterol levels, which is usually an indication of dysfunctional

reverse cholesterol transport. Apo AI, which is the activator of lecithin cholesterol acyltransferase (LACT), is decreased in CKD due to inverse regulation of hepatic Apo AI genes causing a decline in the function of LACT, which leads to decreased cholesterol esterification and abnormality in HDL maturation. The activity of LACT is persistently decreased in CKD, so there is reduced HDL levels.

In a study by MDRD, low HDL levels in CKD patients were one of the independent risk factor for progression of kidney disease. In our study the mean value was significantly lower than the age matched healthy controls.

ELEVATED RIGLYCERIDES

Triglyceride levels were essentially elevated in our study than in control group. Abnormal triglyceride values were found in 13 out of 100 patients in our study. The present study demonstrates that CRF is commonly accompanied by lipid dysfunction manifesting as hypertriglyceridemia.

This is in co-ordinance to the observations made in Western studies and recent Indian studies[60,61,62,63] by Gupta DK,Das BS and Bagdae J. Elevated triglyceride levels are implicated to impaired activity lipoprotein lipase (LPL)[64] and direct inhibitory action of various uremic 'toxins' on the enzymes involved in lipid metabolism[65]

pinpointing the most important pathophysiological mechanisms causing the development of hypertriglyceridemia in renal failure.

Chan MK et al also showed hypertriglyceridemia was the major abnormality in their studies. Hypertriglyceridemia may represent an early feature of renal failure.

ELEVATED LOW DENSITY LIPOPROTEIN & VERY LOW DENSITY LIPOPROTEIN:

LDL was essentially elevated compared to that of controls in our study. We found that 62 of 100 of patients showed elevated LDL levels and in our study 61 out of 100 patients showed raised LDL levels. Most studies point out that Uraemic Patients commonly have normal to slightly decreased concentrations of LDL-C levels and they exhibit significant disturbance in the density distribution of LDL sub fraction that is characterized by presence of predominantly small dense LDL particles.[66]

In the present study, we find significantly high levels of LDL cholesterol in the group with CKD stages IV & V

TOTAL CHOLESTEROL

Total cholesterol levels were raised in 74 out of 100 patients in our study group with CKD results in acquired LDL receptor deficiency, which plays a vital role in the cause of associated hypercholesterolemia. 67

Correlation Studies:

It was found that abnormal serum triglycerides, TC, HDL, were found to be increased significantly in the group of eGFR between CKD stage 3,4,and 5

CONCLUSION

7. CONCLUSION

In my study population, 100 CKD patients who were on conservative line management were studied. Among them 88% the patients had high TSH values,12% had low T3values & 89% had low T4 values.

The modification in the serum levels of T3 and T4 in patients with CKD can be considered protective mechanism, favouring conservation of protein.

There is progressive increase in count of patients with a decreasing T3 and T4 and increasing TSH proportional to the severity of renal failure.

There is also increase in incidence of hypothyroidism found in patients with chronic kidney disease.

As the age progresses, there is increase in incidence of Low T3 syndrome in patients with CKD.

In patients with low GFR the serum T3,T4 levels was found to be low. This shows a direct linear relationship between GFR and T3,T4 levels.

HDL levels were reduced and triglycerides, total cholesterol and TGL levels, LDL, VLDL were raised in the study group in comparison to the controls.

There is a statistically significant rise in the level of serum triglycerides, serum LDL, serum VLDL in CKD grade III,IV and V patients.

There was a negative correlation between serum HDL level and GFR levels which was statistically essential & significant.

All the lipid abnormalities found in CKD were reduced HDL-C levels in serum along with a significant rise in Serum triglyceride, serum cholesterol serum LDL level and serum VLDL level.

ANNEXURES

8. ANNEXURES

PROFORMA

S. No :

Name : Weight :

Age/Sex : Height :

Occupation : BMI :

Address :

History :

Diabetes Mellitus :

Hypertension :

Clinical examination :

Investigations: Ref values

Complete Blood Count:

TC:

DC : P %; L %; E %; M %; B%

TRBC :

Hb :

PCV :

PLT :

ESR : mm in ½ hr

mm in 1 hr

Blood sugar:

Renal function tests:

Bld. Urea : 15-40 mg%

Se. Creatinine : 0.2-1.2 mg%

Serum electrolytes:

Na+	:	135-145mEq/l
K+	:	3.5-5.5 mEq/l

Thyroid function tests (method)		Reference Value
T3	-	0.5-2.0 ng/ml
T4	-	4.4-11.6 IU/L
TSH	-	0.5-7.0 mmol/L

Lipid Profile:

Total cholesterol	-	150-200 mg/dl
Triglycerides	-	70-200 mg/dl
HDL	-	35-60 mg/dl
VLDL	-	0-40 mg/dl
LDL	-	70-130 mg/dl

USG Abdomen & Pelvis:

Other investigations:

Δ: CHRONIC KIDNEY DISEASE - STAGE -

$eGFR=186\times(\text{creatinine in } \mu mol/L/88.4)^{-1.154}\times(\text{age in yrs})^{-0.203} \times (0.742 \text{ if female}) \times (1.21 \text{if black})$

STAGE	eGFR	
1	>90	
2	60-89	
3	30-59	
4	15-29	
5	<15 or on dialysis	

Study of Thyroid and Lipid Profile in

Chronic Kidney Disease

S. No :

Name :

Age/Sex :

Δ :

Renal function tests:

Blood. Urea :

Serum. Creatinine :

Thyroid function tests (method :)

T3- 0.5-2.0 ng/ml

T4- 4.4-11.6 IU/L

Free T3-

Free T4-

TSH- 0.5-7.0 mmol/L

Lipid Profile:

Total cholesterol-	150-200 mg/dl
Triglycerides-	70-200 mg/dl
HDL-	35-60 mg/dl
VLDL-	10-40 mg/dl
LDL-	70-130 mg/dl

நோயாளிகளுக்கு அறிவிப்பு மற்றும் ஒப்புதல் படிவம்
மருத்துவ ஆய்வில் பங்கேற்பதற்கு

ஆய்வு செய்யப்படும் தலைப்பு :
பங்கு பெறுபவரின் பெயர் :
பங்கு பெறுபவரின் வயது :

		புங்கு பெறுவர் இதனை ✓ குறிக்கவும்
1	நான் மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் நான் படித்து புரிந்து கொண்டேன். என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டுள்ளது என அறிந்து கொண்டேன்	☐
2	நான் இவ்வாய்வில் தன்னிச்சையாக தான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும், எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.	☐
3	இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்து மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன்.	☐
4	இந்த ஆய்வில் மூலம் கிடைக்கும் தகவலையோ, முடிவையோ பயன்படுத்திக் கொள்ள மறுக்க மாட்டேன்.	☐
5	இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக் கொள்கிறேன். எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன், ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ, அல்லது எதிர்பாராத, வழக்கத்திற்கு மாறான நோய்குறி தென்பட்டாலோ உடனே இதை மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்கிறேன்.	☐

பங்கேற்பவரின் கையொப்பம் / ..... இடம்.....தேதி.....
கட்டைவிரல் ரேகை

பங்கேற்பவரின் பெயர் மற்றும் விலாசம்.....

ஆய்வாளரின் கையொப்பம் / ..... இடம் ..... தேதி.....

ஆய்வாளரின் பெயர்.....

மையம் .....

கல்வியறிவு இல்லாதவற்கு (கைரேகை வைத்தவர்களுக்கு) இது அவசியம் தேவை

சாட்சியின் கையொப்பம் / ..... இடம் ..... தேதி .....

பெயர் மற்றும் விலாசம் .....

INFORMED CONSENT FORM

Study Title _____

Study Number _____

Subject's Full Name _____

Date of Birth/Age _____

Address _____

1. I confirm that I have read and understood the information sheet dated for the above study and have had the opportunity to ask questions.
   OR I have been explained the nature of the study by the Investigator and had the opportunity to ask questions

2. I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason and without my medical care or legal rights being affected.

3. I understand that the sponsor of the clinical trial/project, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. However, I understand that my Identity will not be revealed in any information released to third parties or published.

4. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s)

5. I agree to take part in the above study

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative: _____

Signatory's Name _____ Date _____

Signature of the Investigator _____ Date _____

Study Investigator's Name _____

Signature of the Witness _____ Date _____

Name of the Witness

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S.NO	NAME	AGE	SEX	SEX CODE	DIABETES	DM CODE	HYPERTENSION	HT CODE	EGFR	CKD GRADE	GRADE CODE	UREA	CREATININE	T3	T4	TSH	TOTAL CHOLESTROL	TGL	HDL	LDL	VLDL
1	KRISHNAMOORTHY	62	MALE	1	+	1	+	1	16	IV	4	100	4.2	1.8	1.22	8.8	120	174	40	125	80
2	MUTHUKUMAR	60	MALE	1	-	2	-	2	66	II	2	84	1.2	1.6	7.6	7.5	195	144	56	145	18
3	CHELLATHURAI	65	MALE	1	+	1	+	1	21	IV	4	135	3.2	0.5	2.2	8.6	210	185	37	128	35
4	HARIKRISHNAN	53	MALE	1	+	1	+	1	16	IV	4	100	4.2	0.7	1.32	8.1	265	175	36	172	43
5	KOVILPITCHAI	68	FEMALE	2	-	2	+	1	68	II	2	102	1.2	1.4	6.5	8.34	170	152	48	120	15
6	KANAPATHI	60	MALE	1	+	1	-	2	15	IV	4	79	4.3	1.1	2.32	11.5	231	167	31	168	21
7	KARIPASAMY	40	MALE	1	+	1	+	1	29	IV	4	116	2.59	1.5	2.54	8.6	210	176	43	125	32
8	SUDALAIMANI	55	MALE	1	-	2	+	1	54	III	3	76	1.48	1.9	3.34	12.2	163	241	32	140	34
9	MURUGAN	54	MALE	1	+	1	+	1	12	V	5	106	5.5	0.7	2.1	10.8	258	203	26	129	80
10	THANGAVEL	39	MALE	1	+	1	+	1	6	V	5	105	10.1	1.2	2.5	14.5	243	204	28	174	65
11	LAKSHMANAN	64	MALE	1	-	2	+	1	55	III	3	74	1.39	1.32	3.1	8.13	195	165	56	142	42
12	GANAPATHY	70	MALE	1	+	1	+	1	45	III	3	87	1.65	1.1	3.7	16.7	210	170	36	140	45
13	KALIAPPAN	42	MALE	1	+	1	-	2	19	IV	4	136	3.8	1	1.56	12.7	235	175	35	153	54
14	AZHAGAR	57	MALE	1	+	1	-	2	25	IV	4	164	2.8	1.8	2.65	10.2	210	173	40	125	65
15	SANJEEVI	56	MALE	1	+	1	+	1	16	IV	4	25	4.1	0.7	4.2	7.12	220	160	38	142	58
16	CHINAMARIMUTHU	50	MALE	1	-	2	+	1	38	III	3	15.6	2	0.9	4.3	7.98	205	135	43	143	41
17	MOHAMMED ISHMAIL	22	MALE	1	+	1	-	2	23	IV	4	21.2	3.6	0.7	2.1	8.09	202	187	34	123	47
18	SANKARAN	53	MALE	1	+	1	+	1	32	III	3	83	2.3	1	4.2	6.6	182	102	29	123	32
19	POOVATHIAMMAL	52	FEMALE	2	+	1	-	2	25	IV	4	204	2.17	1.5	2.43	12.3	228	209	39	125	41
20	SAKTHIVEL	42	MALE	1	-	2	+	1	16	IV	4	150	4.4	0.8	2	7.89	231	190	42	123	38
21	AMALRAJ	39	MALE	1	-	2	+	1	58	III	3	22.6	1.45	1.2	3.3	8.98	195	162	33	122	21
22	SUTHANTHINAKODI	40	MALE	1	+	1	+	1	42	III	3	328	1.9	1	4	8.8	198	170	36	120	34
23	MOHAN	38	MALE	1	+	1	+	1	17	IV	4	99	4.18	0.6	1.62	7.7	235	160	38	142	22
24	MURUGAIAH	51	MALE	1	+	1	+	1	16	IV	4	168	4.2	0.9	1.34	8.8	224	574	42	185	210
25	SADACHARAVEL	44	MALE	1	+	1	+	1	42	III	3	195	1.89	1	4.56	7.67	199	144	50	128	22
26	VINAYAGAM	58	MALE	1	+	1	-	2	20	IV	4	183	3.45	0.7	2.98	8.8	209	230	44	196	46
27	MARY	56	FEMALE	2	+	1	-	2	19	IV	4	156	2.8	1	4.9	6.8	243	198	32	128	32
28	KARUPAYI	50	FEMALE	2	+	1	-	2	12	V	5	292	4.1	0.7	3.4	10.4	278	175	35	180	79
29	paulthai	44	FEMALE	2	+	1	+	1	14	V	5	96	3.76	1.1	2.2	11.6	284	184	34	183	39
30	vijaya	34	FEMALE	2	-	2	-	2	15	IV	4	126.6	3.6	0.6	2.2	109	257	186	34	128	35
31	muthathal	55	FEMALE	2	+	1	+	1	24	IV	4	89	2.22	0.7	3.2	8.5	233	194	32	154	64
32	mohaideen fathima	62	FEMALE	2	+	1	+	1	20	IV	4	94	2.54	0.7	2.1	6.4	254	192	37	125	53
33	suvisesamuthu	62	MALE	1	+	1	-	2	24	IV	4	160	2.85	0.5	2.4	8.3	233	178	39	121	47
34	subbai	51	MALE	1	+	1	+	1	15	IV	4	175.8	4.5	0.7	3.2	6.7	243	178	41	119	39
35	SUBBULAKSHMI	20	FEMALE	2	+	1	+	1	19	IV	4	184	3.3	1.6	2.8	7.4	245	204	32	122	49
36	SANKAR	40	MALE	1	+	1	-	2	14	V	5	143	5	0.8	2.5	10.8	204	214	30	172	67
37	LINGAM	89	MALE	1	+	1	+	1	18	IV	4	165	3.5	0.9	1.84	14.8	156	182	37	168	58
38	PUSHBARANI	44	FEMALE	2	+	1	+	1	18	IV	4	176.9	3	0.7	2.92	9.5	300	176	39	123	57
39	CHINNAPANDI	40	MALE	1	-	2	+	1	34	III	3	173	2.3	0.9	3.4	7.89	204	177	50	154	44
40	MARIAMMAL	35	FEMALE	2	-	2	-	2	16	IV	4	94	3.45	1.6	3.6	9.5	295	184	32	165	68
41	MALATHI	24	FEMALE	2	-	2	+	1	26	IV	4	128.6	2.43	0.8	1.5	11.4	287	204	37	125	46
42	NARAYANAMOORTHY	55	MALE	1	+	1	+	1	20	IV	4	182	3.49	1.2	3.4	12.1	268	184	39	124	44
43	PRIYADHARSHINI	74	FEMALE	2	+	1	-	2	12	V	5	95.7	3.76	0.4	1.9	12.5	238	194	34	173	68
44	YOUSEPH	50	MALE	1	-	2	+	1	15	IV	4	87.6	4.56	0.7	2.54	7.8	194	144	37	173	33
45	ELAMATHI	27	FEMALE	2	-	2	+	1	22	IV	4	162	2.7	0.8	1.76	8.7	202	189	40	126	34
46	VADHINI	39	FEMALE	2	+	1	+	1	15	IV	4	135.7	3.6	0.6	1.54	11.4	190	159	33	175	32
47	POOMARI	50	FEMALE	2	+	1	-	2	16	IV	4	183	3.3	0.9	1.76	9.6	276	210	38	174	31
48	SALARAJAN	25	MALE	1	-	2	+	1	18	IV	4	174	4.4	1.1	2.07	11.3	298	157	32	165	41

49	KUMAR	23	MALE	1	+	1	+	1	42	III	3	113.8	2.1	1.1	3.04	9.6	203	178	33	129	42
50	MALLIKA	40	FEMALE	2	+	1	+	1	12	V	5	103.6	4.5	0.3	2.9	14.5	210	196	30	128	69
51	LAKSHMI	55	FEMALE	2	+	1	+	1	15	IV	4	94.5	3.3	0.9	3	12.6	256	184	36	166	37
52	SORNAM	60	FEMALE	2	+	1	+	1	8	V	5	156	5.5	1.1	3.67	9.4	278	188	35	187	39
53	MUPPIDATHI	45	FEMALE	2	+	1	-	2	15	IV	4	178	3.78	0.9	1.76	14.3	269	159	37	167	43
54	GANESHSANKAR	25	MALE	1	-	2	-	2	46	III	3	146.4	1.9	0.9	4.98	15.3	263	138	38	138	33
55	VAIRAMUTHU	70	MALE	1	+	1	+	1	16	IV	4	159	3.89	1.2	3.76	8.5	274	196	37	128	36
56	RAMALAKSHMI	30	FEMALE	2	-	2	+	1	15	IV	4	103.6	3.79	0.9	4.5	12.2	200	164	34	188	37
57	GAYATHRI	14	FEMALE	2	-	2	+	1	15	IV	4	134	4.5	0.8	1.7	10.5	194	188	40	186	43
58	JANANOSHAN	39	MALE	1	-	2	+	1	21	IV	4	165	3.5	0.9	3.9	7.9	198	207	38	187	53
59	FATHIMA BEEVI	65	FEMALE	2	+	1	+	1	17	IV	4	152	2.89	0.9	4.6	11.4	202	189	39	174	65
60	BASKAR	55	MALE	1	+	1	-	2	35	III	3	89	2.1	0.6	4.7	7.6	200	178	57	175	55
61	RAVIAPPAN	71	MALE	1	-	2	-	2	18	IV	4	193.5	3.5	0.6	2.7	5.8	193	174	37	178	84
62	SHANMUGASUNDHARAM	63	MALE	1	+	1	+	1	27	IV	4	186	2.57	0.8	4.8	11.2	255	126	38	198	54
63	NARAYANAN	45	MALE	1	+	1		1	41	III	3	174	1.89	0.9	2.5	6.8	196	133	33	178	44
64	ARULNATHAN	61	MALE	1	+	1	+	1	23	IV	4	114	3	0.4	3.2	12.6	292	188	31	189	45
65	ANTONYAMMAL	57	FEMALE	2	+	1	+	1	12	V	5	108.5	4	0.7	2.5	9.4	295	185	34	162	66
66	KALYANI	55	FEMALE	2	-	2	+	1	22	IV	4	132	2.45	0.8	3.8	5.8	228	163	36	174	35
67	CHINNASAMY	45	FEMALE	2	-	2	+	1	24	IV	4	175	2.3	0.8	3.9	9.3	256	184	37	163	35
68	ARUNACHALLATHAMMAL	60	FEMALE	2	+	1	-	2	23	IV	4	142	2.3	0.4	2.2	7.9	222	173	40	126	54
69	PANDIAN	64	MALE	1	-	2	+	1	25	IV	4	94	2.7	0.5	2.2	6.8	245	183	36	276	64
70	MUTHUSAMY	45	MALE	1	+	1	-	2	20	IV	4	191.7	3.6	0.8	3.5	8.1	236	185	37	174	64
71	GNANAPRAKASAM	45	MALE	1	+	1	-	2	22	IV	4	132.8	3.3	0.6	3.2	9.3	276	152	34	124	35
72	CHINNAKANNI	49	MALE	1	-	2	+	1	15	IV	4	185	4.4	0.8	2.2	9.5	298	158	33	123	36
73	SANKARVIGNESH	30	MALE	1	+	1	-	2	40	III	3	193	2.1	1.1	2.8	8.7	194	118	56	176	44
74	RAKKAIAH	45	MALE	1	+	1	-	2	19	IV	4	124	3.76	0.9	2.5	7.8	265	159	31	174	37
75	ARULJOYHI	38	FEMALE	2	-	2	+	1	32	III	3	163.7	1.89	0.9	4	6.7	222	173	38	164	45
76	PITCHAMMAL	58	FEMALE	2	+	1	-	2	31	III	3	139	1.8	1	3.7	8.4	204	190	49	142	46
77	SEKAR	49	FEMALE	2	-	2	+	1	14	V	5	152	3.6	0.4	4.2	8.4	203	209	30	179	76
78	MAREAMMAL	50	FEMALE	2	+	1	+	1	18	IV	4	166.5	2.9	0.3	3.2	8.9	198	126	32	163	55
79	KRISHNASAMY	65	MALE	1	+	1	-	2	19	IV	4	182	3.5	1.3	1.8	12.5	194	190	33	175	43
80	THIRUMANI	52	MALE	1	+	1	-	2	15	IV	4	163	4.5	0.4	1.08	6.7	243	173	36	123	76
81	SIVAMURUGAN	40	MALE	1	-	2	+	1	25	IV	4	117.8	3	0.6	2.87	8.6	254	134	37	163	85
82	ESWARAPILLAI	54	MALE	1	-	2	+	1	26	IV	4	162	2.7	0.8	3.35	9.5	265	173	38	121	556
83	SENTHILKUMAR	45	MALE	1	+	1	-	2	41	III	3	159	1.9	0.9	4	7.6	232	112	49	122	45
84	MARIMUTHU	27	MALE	1	+	1	+	1	17	IV	4	132.8	4.4	0.4	2.3	9.5	245	142	35	154	34
85	MUTHULAKSHMI	29	MALE	1	+	1	+	1	24	IV	4	183	3.27	1.1	3	13.2	273	175	33	132	23
86	KANAGAMANI	45	FEMALE	2	-	2	+	1	12	V	5	172	4.4	0.9	1.34	14.6	275	213	32	168	38
87	MOHAMED HASIM	10	MALE	1	+	1	+	1	45	III	3	96	2.3	0.8	3	7.3	199	194	34	165	31
88	CHINNATHAMBI	45	MALE	1	+	1	+	1	19	IV	4	104.7	3.7	0.4	0.6	9.8	206	156	35	158	54
89	ARUMUGAM	39	MALE	1	+	1	+	1	16	IV	4	119	4.3	1.1	0.2	6.4	265	174	35	173	37
90	KANNAN	45	MALE	1	-	2	+	1	13	V	5	179.5	5.1	0.9	0.6	9.8	297	179	25	125	74
91	GANESHAN	45	MALE	1	-	2	+	1	33	III	3	126	2.3	0.9	5	11.7	198	184	15	165	43
92	RAKKAIAH	45	MALE	1	-	2	+	1	17	IV	4	94	4	0.6	0.78	14	198	173	38	156	48
93	VELLAMMAL	55	MALE	1	-	2	+	1	17	IV	4	105	3.9	0.7	4.45	11.8	243	147	39	129	59
94	SAMUTHIRAPANDI	63	MALE	1	+	1	-	2	22	IV	4	193	3.1	0.5	3.4	6.9	276	146	38	119	65
95	ARUNACHALLAM	65	MALE	1	+	1	-	2	24	IV	4	153	2.8	0.3	2.2	8.5	254	185	38	121	43
96	SELVAM	50	MALE	1	-	2	+	1	15	IV	4	129.8	4.5	0.9	4	7.9	234	165	31	121	29
97	SOLAIAMMAL	49	FEMALE	2	+	1	_	2	24	IV	4	99	2.3	1.1	2.4	7.9	198	174	32	142	34
98	KALA	60	FEMALE	2	-	2	-	2	15	IV	4	152.6	3.6	0.4	3.4	7.6	276	154	33	165	23
99	ARUMUGAM	46	MALE	1	+	1	+	1	17	IV	4	198	4	0.3	0.43	8.4	243	173	35	158	54

100	JOSEP	50	MALE	1	+	1	+	1	57	III	3	163	1.39	0.7	4.2	7.5	189	182	37	125	34